THE SURGICAL CLINICS OF NORTH AMERICA

DECEMBER 1979

MORBID OBESITY

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THE SURGICAL CLINICS OF NORTH AMERICA

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SYMPOSIUM ON
MORBID OBESITY

Henry Buchwald, M.D., *Guest Editor*

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Foreword

Morbid obesity is not only a medical disease, it is also a serious social, psychological, and economic problem. In society today, grotesque adiposity is in the ascendency and penetrates all socioeconomic levels. Those individuals so afflicted cannot be regarded as curiosities. They must be considered to be most unfortunate persons who are entitled to the best efforts of the medical profession.

This issue of *Surgical Clinics of North America* has as its dual subjects the disease of morbid obesity and its current management. Each of the 18 chapters was written by an expert or by a group of experts in the field; indeed, many of the authors are responsible for the clinical contributions they espouse. The reader will readily ascertain that certain deductions (e.g., the etiology of morbid obesity) and recommendations (e.g., the operative therapy of choice) clash. This is as it should be in an evolving field that is attempting to establish hard data. Doubt and exploration, not necessarily consensus, are the pillars of scientific inquiry. We must avoid rushing to make a judgment, and instead cooly assess the stream of publicity (often in the lay press) on yet another variation of a previous operation that now promises "dramatic results free of complications." These panaceas, as a rule, do not withstand the test of time.

All surgical approaches to the management of morbid obesity are an approximation to rational therapy, since surgeons do not, at this time, deal with the primary etiology of this disease. A rerouting of the intestinal tract is metabolic surgery, not an attack on the cause of the problem. My own conviction, based on currently available genetic, experimental, and psychological-psychiatric data, is that morbid obesity is a metabolic disease with a neuro-humoral basis and a strong hereditary predisposition. Obviously, opportunities for research on the cause or causes of morbid obesity are protean, and future therapy will have to be based on a knowledge of mechanisms.

Certainly, this volume is not exhaustive in regard to studies of the cause, physiology, and biochemistry of morbid obesity. The discussion of therapy, however, tends to be exhaustive in the emphasis on the surgical approach. There are variations of jejunoileal bypass or gastric procedures that could have been represented; the surgical approach to management, however, is basically limited to these two sets of interventions. There are today no recommendable operations on the endocrine or

neurologic systems to modify morbid obesity. More strikingly, there are no nonoperative—diet (with or without support analysis and counselling) or drug—approaches to morbid obesity that offer even a modicum of success or promise. Some have spoken of operative therapy in this area as radical. Possibly so, but, more to the point, surgery is the only currently reasonable therapy. Herein lies the challenge.

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Definition and Health Consequences of Morbid Obesity

*Ernst J. Drenick, M.D.**

This volume is designed to deal primarily with the problems and the surgical treatment of morbidly obese patients. Historically, assessments of survival risk and longevity have been the domain of the insurance industry. While obesity of mild to moderate degrees has been investigated from every conceivable angle, comparatively little is known regarding the particular problems, risks, morbidity, and mortality in the uninsurable morbidly obese.

A number of casual observations have made physicians aware of the health hazards and of the likelihood of a shortened life span. For instance, it is relatively rare to see in public elderly people who are truly morbidly obese. In fact, it is younger and middle-aged persons in whom morbid obesity is more commonly encountered, and when ill, a disproportionate number seem to be admitted to intensive care units. Consequently, suspicion must arise that morbid obesity shortens the life span.

Because overall information on gross obesity is tenuous, some of the views expressed in this article are, to a certain extent, subjective, and the factual data had to be based on the experiences in limited numbers of patients.

Etiologic Mechanisms

Obesity of any degree is the consequence of a positive energy balance. In theory, a moderate consistent excess of food, or a decrease in physical work, or an element of increased metabolic efficiency peculiar to the obese, may singly or in combination contribute to a weight gain. However, in the grossly obese, the primary cause is almost always a very large food intake. It has been convincingly shown in metabolic research units that an individual in the 160 to 200 kg range must eat in excess of 6000 calories per day to keep from losing weight.

Many theories have been proposed as explanations for the phenomenon of pathologic food consumption. Clearly, the morbidly obese do not, as a rule, eat because they are physically hungry, nor do they overeat

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because the food is tasty. Most morbidly obese are true addicts. What actually distinguishes a potential food addict in his or her emotional make-up from a person with normal eating habits is unknown. Certain extranenous influences appear to favor a trend to a pattern of overeating. For instance, gross obesity in parents commonly generates poor food habits in the offspring. Enforced deprivation, as might occur in prisoner of war camps, can precipitate excessive consumption of food and gross obesity following liberation. How much an existing genetic predisposition to fatness contributes to the development of gross obesity is not clear either, but it may well represent a prime etiologic mechanism in some individuals. On the other hand, there is no convincing evidence that genetic predisposition toward fatness leads to an increased incidence of frank, morbid obesity.

The abundance of food in Western society, the increasingly sedentary life style, and cultural practices in racial and ethnic groups can help promote obesity. A neverending search continues for proof of some biologic abnormality which might explain why one individual becomes obese while another does not, although both are seemingly equally active and eat equally large quantities of food. So far, none of the many documented abnormalities in metabolism, in hormonal control, or in physiological function present in gross morbid obesity have persisted after such individuals reduced to normal weight. While minor quantitative differences in metabolic efficiency are obviously discernible when lean and moderately obese subjects are compared, these do not satisfactorily explain the development of morbid obesity.

Whether morbid obesity has developed in childhood, adolescence, or in adult life, successful weight reduction by medical means is almost invariably transient and regain is the rule. In Western society and in most developed countries, compulsive overeating is, for all practical purposes, the sole cause of truly morbid obesity. The rates of gain or regain in compulsive eaters are generally rapid. Obesity often worsens in spurts, presenting further proof that massive quantities of food are consumed.

Admittedly, severe obesity may occur in a variety of organic central nervous system disorders but these are extremely rare. In general, such persons are not considered to be suitable candidates for surgical treatment. Hypothyroidism and Cushing's disease may be associated with mild to moderate obesity, but by themselves virtually never lead to morbid obesity. If hypothyroidism is diagnosed in a morbidly obese patient it is, at best, coincidental and correction to a normal metabolic rate fails to bring about a significant weight loss. Non insulin-dependent diabetes of adult onset is frequently associated with moderate obesity, but it rarely causes obesity of a morbid degree. Consequently, control of diabetes with oral hypoglycemics in the grossly obese rarely leads to normalization of weight.

Criteria and Definition of Morbid Obesity

No generally accepted definition for the term "morbid obesity" has been developed. One of the difficulties rests with the assessment of degrees of obesity. Numerous formulas have been applied in an attempt

to improve precision in the measurement of the excess adipose mass. To this end, the concept of Body Mass Index in which weight (kg) is divided by height $(m)^2$ has been proposed and is now used widely in epidemiologic surveys and in scientific publications. Synonyms for this term are the "Obesity Index" and the "Quetelet Index." Others have proposed the use of the "Ponderal Index" calculated as height in centimeters divided by the cube root of the weight in kilograms. In Europe, another formula, the Broca Index, is widely employed. This measurement is obtained by the formula: weight (kg) minus height (cm) minus 100. In the Tecumseh Study, still another method, using skinfold thickness, height, and weight, led to a value termed the Adiposity Index:

Men:

$$0.34 + 226\frac{W}{H^2} + 0.00740 \text{ (subscapular plus triceps skinfold thickness in mm)}$$

Women:

$$0.34 + 242\frac{W}{H^2} + 0.00571 \text{ (subscapular plus triceps skinfold thickness in mm)}$$

A commonly used criterion for morbid obesity has been a flat 100 pound excess over desirable weight. This is a very arbitrary and dubious way of judging obesity. With this appraisal, a 200 pound female who should weigh 100 pounds is 100 per cent over desirable weight, whereas a man weighing 300 pounds who should weigh 200 pounds, carries an extra 100 pounds, but is only 50 per cent over desirable weight.

The conventional and still most widely applied measure of obesity expresses overweight in per cent of desirable weight for age, sex, height and "body frame." Although not very exact and possibly fraught with error in cases of minor degrees of weight excess, this approach has a number of advantages. First, the concept of percentage overweight is easily understood by the layman. Second, changes in weight and in per cent excess move in the same direction, which is not the case with some of the other indices. Third, the innate error of this modality in the grossly obese becomes less significant the greater the excess adipose mass. A simple criterion for the presence of morbid obesity is a weight twice the ideal or more. The ideal weight can easily be calculated by assuming a base line weight of 105 to 110 pounds for a five foot individual and adding five pounds for each inch over five feet in height plus five pounds for a medium and ten pounds for a heavy framed subject.

In Table 1, the respective obesity indices as applied to one grossly obese female and a grossly obese male are shown to permit comparisons. For scientific purposes, the Body Mass Index has become the most widely used measurement. This index offers the advantages of an independent measure of relative weight.

To establish the term "morbid obesity" in a context of clinical relevance, it appears that this designation should be reserved for those degrees of obesity which can clearly be shown to correlate with an unquestioned excess in morbidity or mortality. For the younger and middle-aged groups, a decisive (60 per cent) excess mortality becomes evident

Table 1. *Comparison of Different Methods to Measure Obesity*

	PER CENT OVERWEIGHT*	BODY MASS INDEX $\frac{\text{wt (kg)}}{\text{ht}^2\text{ (m)}}$	PONDERAL INDEX $\frac{\text{ht (cm)}}{\sqrt[3]{\text{wt (kg)}}}$	BROCA INDEX wt (kg)–ht (cm)–100
Male 5′ 10″ (179 cm) 300 lbs. (136 kg)	67.7	43.07	10.5	58.30
Female 5′ 5″ (150 cm) 250 lbs. (124 kg)	66.7	41.60	10.3	48.30

*Adapted from Metropolitan Life Insurance Co.: New weight standards for men and women. Statistical Bulletin, 40:3, 1959.

when the relative overweight is 60 per cent above normal or greater. Since mortality is ultimately an expression of morbidity, a reduction in morbidity is a valid goal of treatment. Therefore, it becomes important to identify the various pathologic sequelae or concomitants of obesity which can be improved or eliminated with weight loss.

Prevalence of Gross Obesity

No reliable data are available on the prevalence of morbid obesity in the United States. Data from the First Health and Nutrition Examination Survey, United States (1971–1974) indicated that among men aged 21 to 74 years, 4.9 per cent or about 2.8 million were "severely" obese. For women, the figures were 7.2 per cent or about 4.5 million. It should be noted, however, that severe obesity in this survey was considered to be any weight greater than 244 pounds for men and any weight greater than 225 pounds for women. Less than 0.1 per cent of the U.S. female population weighed more than 250 and less than 0.1 per cent more than 300 pounds.

Increased Mortality

A number of studies have dealt with the increased mortality associated with overweight, but published statistics appear to have underestimated the seriousness of the problem. In the Study on Build and Blood Pressure by the Society of Actuaries in 1959,[19] a mortality ratio of 168 per cent of expected was calculated for insured males weighing over 254 pounds (115 kg). Since an insured population is selected among better risks, the true mortality of a randomly observed group may well be greater.

In a Veterans Administration study of 200 morbidly obese men, aged 23 to 70 years, with an average weight of 143.5 kg, the mortality in comparison with that among normal males in the general United States population, demonstrated a 12-fold increase in the age group 25 to 34 years and a six-fold increase at ages 35 to 44. The ratio diminished with advancing

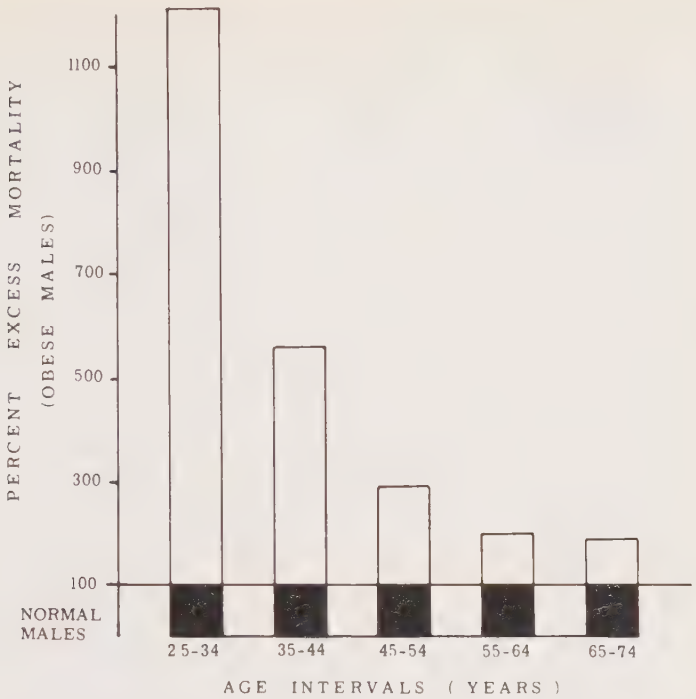

Figure 1. Excess mortality of morbidly obese males over that of the general U.S. male population. (*From* Drenick, E. J., Bale, G. F., Seltzer, F., et al.: Excessive morbidity and causes of death in morbidly obese man. J.A.M.A., in press, with permission.)

age (Fig. 1). During the average follow-up period of 7.6 years, 50 of the original group of 200 subjects had died. As one might expect, the weight excess of those who died was somewhat greater. However, there were no differences between the survivors and those dying in age, duration of obesity, or whether obesity developed first in childhood or in adult life.

In a collection of several reports it was asserted that of 16 patients who weighed over 300 kg only two lived past 39 years of age. An assessment of survival in a West German study recently determined that the overall life span for the obese population was reduced by four years and for the population developing cancer by two years.

Data from the new Build and Blood Pressure study confirm the association of gross (but not morbid) obesity and increased mortality.[9] For men 40 per cent above desirable weight, excess mortality from all causes amounted to 50 per cent. For specific disease entities the increased mortality was 60 per cent for cardio-cerebro-vascular disorders, 120 per cent for digestive diseases, and more than 400 per cent for diabetes. This last example is not entirely pertinent since in this statistic, diabetes may have been present as the primary condition.

The causes of death in the Veterans Administration study were of interest because they reflected specific risk factors. Figure 2 compares the causes of death in the group under study, identified from hospital records or death certificates in 46 of the subjects, with those in the United

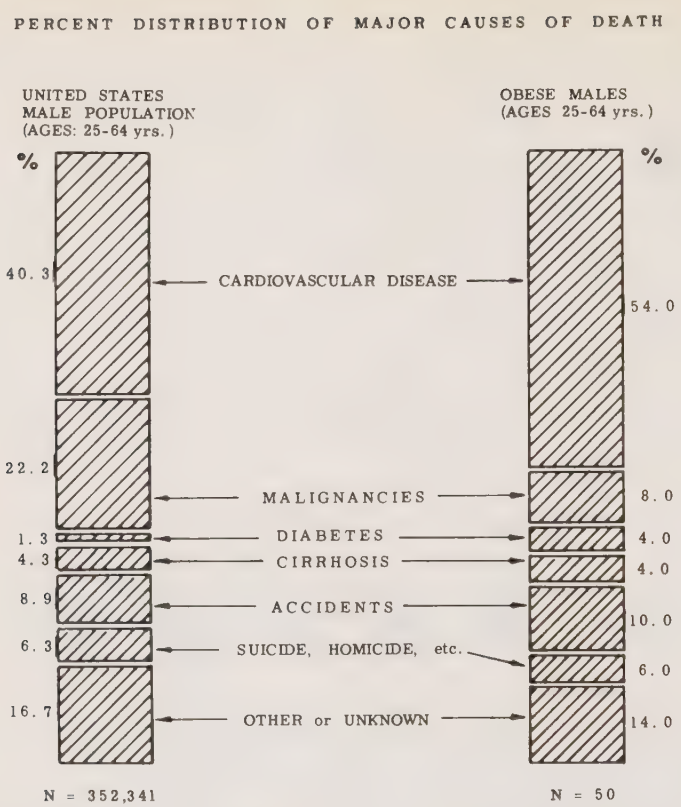

Figure 2. Major causes of death in morbidly obese males compared to U.S. male population. (*From* Drenick, E. J., Bale, G. F., Seltzer, F., et al.: Excessive morbidity and causes of death in morbidly obese man. J.A.M.A., in press, with permission.)

States male population. Cardiocerebrovascular deaths were almost 30 per cent higher in the obese. Neoplasms were less frequent, presumably because of the many deaths at a relatively early age. Only one patient died of cardiopulmonary failure, considered to be the direct consequence of morbid obesity. Two patients choked on food during eating sprees and suffered respiratory arrests. In addition to these two avoidable episodes, the number of fatal accidents was surprising. Deaths resulted from drowning in a flooded river bed, gunshot, automobile crashes, and drug overdose. Considering that most morbidly obese are not exposed to some of the risks of a physically active male population, one would have to conclude that being overweight made these patients less alert, less mobile, and more vulnerable to unforeseen physical dangers.

Since only a few deaths could be termed immediate and proximate results of obesity, additional factors rather than the mere presence of disease must have contributed to the fatal outcome. Thus, it appears that the obese state caused the commonly occurring degenerative diseases to begin at an earlier age, to progress more rapidly, and to become life-threatening more frequently.

Other elements enter into the picture. Because of past disappoint-

ment and frustration, obese patients are notoriously reluctant to seek medical attention. Precise diagnoses in any number of illnesses are more difficult in the presence of gross obesity and, therefore, prompt and appropriate treatment is frequently delayed. Finally, relatively benign conditions in patients of normal weight often cause critical illnesses in the grossly obese. It is the obesity, then, rather than an unusual spectrum of illnesses which causes the excessive mortality.

The Pickwickian or Obesity-Hypoventilation Syndrome

The obesity hypoventilation syndrome is virtually the only disorder in which the excess adipose mass, in the absence of any other contributing factors, can lead to death. Cardiopulmonary failure ensues relatively rarely in the morbidly obese. It developed in only 8 of 200 men in the Veterans Administration study. MacGregor reported that almost one-third of 22 patients admitted to a hospital with this syndrome died.[10] If treated successfully, these patients can be restored to normal cardiorespiratory function after a relatively modest weight loss. Regain beyond a certain individual threshold causes a recurrence of respiratory insufficiency.

Because aggressive treatment saves many patients, the syndrome now causes surprisingly few deaths. However, even in its milder form, somnolence presents a very real hazard both to the patient and to others. Involvement in traffic collisions is not infrequently reported by morbidly obese patients. The tendency to fall asleep at the wheel is well recognized. For example, one patient seen recently admitted to having caused nine serious accidents.

Risk from Disorders Associated with Obesity

In the great majority of fatal or serious diseases in the obese population, morbidity is the result of the obesity plus one or more pathologic states which interact to cause increased rates of mortality.

A long list could be presented of illnesses associated with obesity which appear to worsen with increasing degrees of overweight and to improve with progressive weight loss. It is in this area particularly that considerable uncertainty exists as to the significance of specific risk factors for males and females at various ages.

Gallstone Disease

An excess incidence of gallstone disease in proportion to overweight has been most clearly demonstrated. The direct correlation is true for males and females alike. In older subjects the incidence is greater. Gallbladder disease was present in close to 35 per cent of 100 per cent overweight women aged 45 to 55 years.[16] Although rarely a cause of death by itself, the need for operative intervention creates an increased risk for the severely overweight individual.

Heart Disease

There seems little doubt that in the obese, and particularly in the morbidly obese, several risk factors are distinctly related to accelerated

atherogenesis. The role of overweight as an independent factor remains controversial, however. Keys found that weight did not contribute to ischemic heart disease when the influence of age, high blood pressure, high serum cholesterol, and smoking were taken into account.[8] This study and several other prospective epidemiologic surveys did not address the problem of atherogenesis in the morbidly obese.[7, 15, 18] With moderate obesity the incidence of coronary disease has been shown to be proportional to degrees of adiposity. Of interest is the observation that the increased incidence of angina, myocardial infarction, and sudden death was highest for overweight men in the age group under 40 years. For women, overweight presented a much smaller risk of untoward cardiovascular events.

In the Veterans Administration study of 200 ambulatory, morbidly obese men, the incidence of probable but symptomless cardiovascular disease was just under 10 per cent. In the course of seven years of follow-up, 26 patients or 13 per cent of the group had died of cardiovascular disease.

The frequent occurrence of a fatal outcome in this group denotes the gravity of coronary disease in the presence of morbid obesity. While coronary disease and its clinical consequences appear to be the combined effects of several risk factors, it is difficult to quantitate the influence of individual risk factors in the morbidly obese.

Serum Cholesterol and Triglyceride as Risk Factors

Hypercholesterolemia has been reliably shown to increase in proportion to overweight only in the moderately obese. In the morbidly obese men of the Veterans Administration study, a slight negative correlation has actually been demonstrated. Surprisingly low serum cholesterol values are frequently seen in extremely obese males and females. One must therefore conclude that atheromatous changes in the coronary arteries as a result of hypercholesterolemia occurred sometime during the evolution of obesity in its less severe stages, or that progressive atherosclerosis in the obese may develop despite normal or low normal cholesterol levels.

Whether or not weight loss by dietary restriction results in a lowering of cholesterol levels is also unclear. During the phase of active weight loss, there generally is a demonstrable decrease in cholesterol levels, but after stable reduced weight has been achieved and maintained, cholesterol tends to return to original levels despite a lower weight. Thus, there is no convincing evidence that serum cholesterol levels correlate with increased mortality in the morbidly obese.

Hypertriglyceridemia is common in obesity owing to an increase in very low density lipoprotein-triglyceride. However, normal or low normal values are not at all infrequent. The contribution of hypertriglyceridemia as a risk factor in atherosclerosis in the morbidly obese appears to be unsettled.

Reductions in serum triglyceride levels during weight loss do occur but generally are relatively minor in degree except in type IV hyperlipoproteinemia. It is unproven and uncertain whether a significant beneficial antiatherogenic effect can be attributed to such changes.

Hypertension

Severe or malignant hypertension appears to be no more common in the morbidly obese than in the nonobese population, and hypertension alone is rarely the primary cause of death. However, hypertension at any age and even of mild degree is one of the major factors contributing significantly to atherosclerotic heart disease in the lean as well as in the obese. The mechanisms leading to a rise in blood pressure in the obese population are not understood. Excessive salt intake may be involved and increased peripheral resistance resulting from unknown causes has been implicated.

A rough correlation has been established, indicating that each 10 kg increase in weight produces a 3 mm increase over baseline in systolic and 2 mm Hg increase in diastolic blood pressure.[1] Hypertension in males is nearly twice as common as in females. Of interest is the observation that with the central "android" distribution of adiposity, hypertension has been found more frequently, and this distribution pattern of adiposity is also more frequent with adult onset obesity. The overall incidence of arterial hypertension has been determined in numerous studies, and inexplicably varies greatly. Although it was not defined by quantitative criteria, Jörgens found a 71 per cent incidence in massively obese patients in Germany.[6] In a study in Italy of grossly obese patients, 12 per cent of females and 60 per cent of males had hypertension.[11]

In the Veterans Administration study group of grossly obese patients, hypertension was also shown to be age-related up to the fiftieth year, and the 65 per cent prevalence for the group was comparable to that in other studies (Table 2). For females this pattern was not evident nor could a weight-related increase in hypertension be demonstrated for males or females (Table 3). The reason for this phenomenon, which conflicts with the observations of others, is unclear. The frequency of severe hypertension was five-fold higher in males.

The benefit of weight loss in achieving a reduction of blood pressure in

Table 2. *Percentage Prevalence of Diastolic Hypertension in Morbidly Obese Subjects*

AGE IN YEARS	>90 mm Hg	>100 mm Hg	>110 mm Hg	PREVALENCE (PER CENT)
Males (N=199)				
<30	2.5	2.5	1.5	6.5
30–40	5.5	7.5	6.5	10.5
40–50	9.0	6.0	11.6	26.6
>50	5.5	4.0	3.0	12.5
All ages	22.5	20.0	22.6	65.1
Females (N=148)				
<30	8.1	2.7	1.4	12.2
30–40	12.2	5.4	2.0	19.6
40–50	6.8	3.4	1.4	11.6
>50	2.0	4.7	0	6.7
All ages	29.1	16.2	4.8	50.1

Table 3. *Percentage Prevalence of Diastolic Hypertension in Two Ranges of Overweight*

WEIGHT EXCESS (PER CENT)	>90 mm Hg	>100 mm Hg	>110 mm Hg
Males (N=99)			
50–100%	17.1	15.1	11.0
>100%	5.5	9.0	7.0
Females (N = 148)			
50–100%	16.2	8.8	1.4
>100%	12.9	6.8	4.0

about half the patients has been demonstrated in many studies. The systolic blood pressure is more readily lowered than the diastolic.

Obesity and Diabetes

While the frequency of obesity in patients with diabetes has been amply documented in numerous studies, much confusion and many conflicting opinions persist with regard to the risk that obesity diabetes imposes upon the individual.

In the grossly obese male population in the Veterans Administration study with a mean age of 42 and with gross obesity of 25 years' duration, about 54 per cent manifested either frank or chemical diabetes mellitus. Since all of these patients had passed physical examinations to enter the armed services, they had not had diabetes or gross obesity 20 to 25 years earlier. Thus, it appears that it takes at least 20 to 25 years of gross obesity to provoke diabetes in 50 per cent of the morbidly obese population. In a grossly obese population in Italy with an average age of 39 and a body mass index of 40.2, Mancini found an incidence of frank diabetes in 16 and chemical diabetes in 36 among 79 males.[11] This represents an incidence of 30 and 46 per cent respectively. For females the frequency of diabetes was lower. Sixteen of 227 had frank diabetes and 40 had chemical diabetes. This reflects a 7 per cent incidence for overt diabetes and an 18 per cent incidence for chemical diabetes.

It seems clear from the various studies that both the incidence and the severity of glucose intolerance increase with age, with the duration of obesity, and with the degree of overweight. The abundant food intake imposes an inordinate stress on the capability of the islet cells to produce insulin and makes them more vulnerable to injury. Second, the mass of enlarged fat cells with a diminished number of insulin receptors causes increased resistance to the insulin effect. In concert, these factors promote the genesis or the aggravation of diabetes in the obese.

In the view of many observers, obesity diabetes alone has not caused the gamut of complications of insulin dependent, adult onset diabetes. Also, it has been generally held that the patient with obesity diabetes is resistant to ketoacidosis. Many obese patients, in fact, tolerate severe hyperglycemia without overt symptoms and do not benefit to a significant degree from exogenous insulin.

The occurrence rate of typical diabetic vascular events is low in the

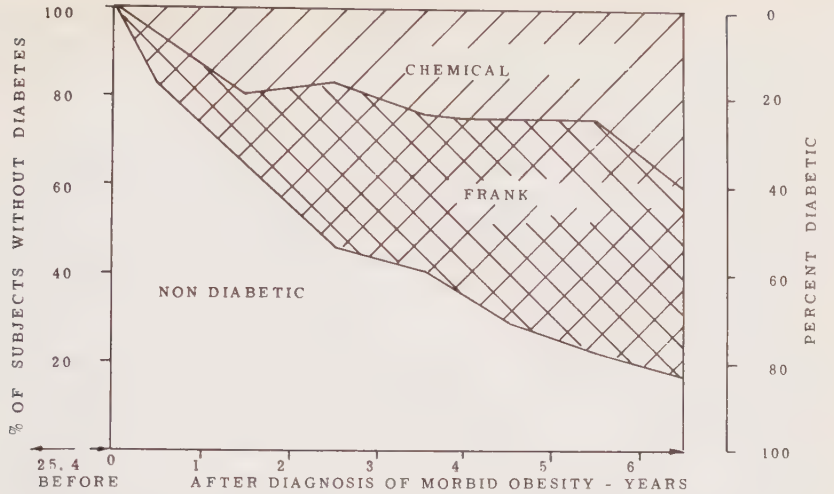

Figure 3. Diabetes developing in the aftermath of weight reduction in previously non-diabetic men with long-standing morbid obesity.

morbidly obese who become diabetic only after many years of gross obesity. In obesity diabetes, amputations, severe renal disease, or blindness are rarely seen. A very drastic departure from the pattern of the usual very gradual and slow development of impaired glucose tolerance over a period of 25 years of obesity, and from the relatively benign form of diabetes, has been noted in obese patients who have lost a great deal of weight but then proceed to regain rapidly. In Figure 3 a disproportionately sudden evolution from normal to abnormal glucose tolerance occurred in 80 per cent of a group of obese patients within six years after normalization of weight and subsequent rapid regain.

The only instances of grave ketoacidosis in morbidly obese patients with diabetes developed following rapid regain, and these fatal events were the consequence of diabetes as the sole etiologic mechanism.[23] The excess mortality due to diabetes, evident in the list of causes of death, presumably has its origin in this particular complication. In addition, the presence of diabetes contributed to the excess mortality as a cofactor in the genesis of cardiocerebrovascular deaths and possibly in the mechanisms leading to thromboembolic and infectious diseases, and may be involved in the evolution of hyperlipoproteinemia. Clearly, weight loss in the obesity diabetes syndrome brings about improvement in glucose disposal and in the effectiveness of insulin, and normalizes the patterns of basal and stimulated insulin secretion.

Risks of Surgery

In grossly obese women weighing more than 300 pounds, the operative mortality following surgery for uterine neoplasms was 20 per cent versus 2 per cent for those between 200 and 250 pounds.[14] In this connection it is worth mentioning that carcinoma of the endometrium was found in 4.0 per cent of obese women with a body mass index of 50.2

versus 0.2 per cent in the lean,[12] representing a 20-fold greater risk for the obese. The risks of surgery and anesthesia, in general, will not be discussed here, since operative treatment is the topic of other articles in this volume.

Pregnancy and Massive Obesity

The outcome of pregnancy in massively obese women (50 per cent above ideal weight according to standard insurance tables) was evaluated by Edwards et al.[5] Mild pre-eclampsia, hypertension, inadequate weight gain (under 12 pounds), pregnancy diabetes, and wound infections were more frequent. Infants with birth weights over 4 kg were born in 21 per cent of deliveries versus 6 per cent for nonobese women. Delivery by cesarean section was much more common in obese women (5.5 per cent) than in lean (0.7 per cent), and consequently complications were frequent in the obese.[13] Women weighing 90 kg or more had a greater incidence of longer pregnancies (greater than 294 days in 9.5 per cent of women), and the miscarriage rate was almost double that for women of normal weight. Babies of obese women had a mortality of 3.5 per cent compared to 1.4 per cent for those of normal women.

Ill-Defined Risks

The list of hazards threatening the survival of the morbidly obese should include a number of other illnesses or events that have not been explored in sufficient detail to permit comparisons of prevalence. Massive pulmonary emboli, sudden death without explanation, acute pancreatitis, serious psychiatric diseases, suicide or unintended deaths from drug overdoses, and a great variety of accidental deaths appear to be more common in the morbidly obese than in the nonobese population.

Risks of Medical Weight Loss Regimens

In the treatment of gross refractory obesity, radically restricted dietary regimens have been employed on a large scale. Moreover, a variety of drugs have been added by some practitioners, possibly accentuating the potential risks associated with rapid weight loss. Little information on the hazards of the refeeding period is available, but certain ill effects have been described following the reintroduction of normal quantities of food. Beyond this, the common occurrence of rapid regain may itself carry certain risks. If the individual patient has certain underlying disorders, the potential for complications appears to be greater.

Total fasting has been blamed for a few isolated deaths. In most of these, the patients had underlying medical disorders or were given diuretics which may have accentuated fast-induced electrolyte disturbances. Lactic acidosis was thought to be responsible in one instance. Terminal cardiac arrhythmias or fragmentation of myofibrils, seen at autopsy, implicated primary cardiac disease as the cause of death.

Recently, poor quality protein products consumed daily in minimal quantities have been recommended as the sole nutrient in a modified fasting scheme. Hydrolyzed collagen, notoriously low in nutritional value, served as the source of protein in many of the commercial products.

Prolonged use may result in deficiency states or in an imbalance of amino acids although the exact nature of the disorder associated with this protein remains obscure.

In 1977 and up to mid-1978, 58 unexpected deaths occurred in 39 young or middle aged obese women and in 19 men who used "predigested protein" for weight reduction. In 16 of these who were otherwise healthy, sudden cardiogenic deaths were documented. The energy intake per day had averaged 300 calories. Vitamin and mineral supplements had been used. The mean treatment period was five months, and the average weight loss 38 kg (83 pounds). Six women had actually started a refeeding regimen shortly before death.

Syncope preceded the fatal episodes. In 10 subjects who died under medical supervision, ventricular tachycardia or fibrillation, refractory to the usual antiarrhythmic drugs was noted. No conclusive evidence of any specific myocardial abnormalities was detected on autopsy.

Epidemiologic studies suggested that the death rate of obese women consuming the liquid protein diet was 30 times greater than that of the general U.S. female population of the same age range.

Although unlikely to result in fatalities, a number of serious ill effects of medical weight loss regimens have been reported. Ketogenic diets may precipitate hyperuricemia and cause gout, urate nephrolithiasis, and, rarely, renal insufficiency.[32] Polyneuritis, peroneal palsy,[17] and Wernicke's syndrome[4] have been reported with fasting and semi-starvation. Thiamine deficiency has been the cause in some of these cases; in others, no clear explanation has been found. Fluid and electrolyte losses during strenuous dieting may lead to hypotension and severe postural changes. These present a serious hazard to patients with pre-existing ischemic disease of brain or heart.

Brief mention should be made of the use or misuse of thyroid and digitalis preparations in the conduct of weight loss regimens. Serious incidents and fatalities have occurred, particularly when these drugs were prescribed in addition to amphetamines. With refeeding, sodium and fluid retention may provoke congestive heart failure in patients with unsuspected cardiac disease. Instances of pancreatitis have been reported.

Summary

A great many factors contribute to the complexities of risk to health and survival of the morbidly obese. An assessment of the social, economic, and psychological handicaps associated with gross obesity is outside the scope of this discussion, although these aspects greatly add to the diminished "quality of life" and therefore, in some measure, to the more serious threats to health and survival in the form of organic illnesses.

Considering the physical hazards and shortened life expectancy the morbidly obese person must face, means to effect a lasting normalization of weight are indicated early in life. Any approach which promises an improved survival with lesser morbidity is a welcome alternative to untreated obesity or to transient, repeated episodes of weight loss by medical means. Permanent relief of morbid obesity has clearly ameliorated many impairments associated with obesity, and offers the probability of a greatly improved quality of life for the individual and a gain for society.

REFERENCES

1. Bjerkedal, T.: Overweight and hypertension. Acta Med. Scand., *159*:13, 1957.
2. Drenick, E. J.: Hyperuricemia, acute gout, renal insufficiency and urate nephrolithiasis due to starvation. Arthritis Rheum., *8*:988, 1965.
3. Drenick, E. J., and Johnson, D.: Evolution of diabetic ketoacidosis in gross obesity. Am. J. Clin. Nutr., *28*:264, 1975.
4. Drenick, E. J., Joven, C. B., et al.: Occurrence of acute Wernicke's encephalopathy during prolonged starvation for the treatment of obesity. New Engl. J. Med., *274*:937, 1966.
5. Edwards, L. E., Dickes, W. F., Alton, I. R., et al.: Pregnancy in the massively obese: Course, outcome and obesity prognosis in the infant. Am. J. Obstet. Gynecol., *121*:479, 1978.
6. Jörgens, V., Berchtold, P., et al.: History, clinical and metabolic findings in 500 massively obese patients (abstract). Int. J. Obesity, *2*:482, 1978.
7. Kannel, W. B., Le Bauer, E. J., et al.: Relation of body weight to coronary heart disease: The Framingham Study. Circulation, *35*:734, 1967.
8. Keys, A., Aronovis, C., et al.: Coronary heart disease: Overweight and obesity. Ann. Intern. Med., *77*:15–27, 1972.
9. Lew, E. A., and Garfinkel, L.: Variations in mortality by weight among 750,000 men and women. J. Chron. Dis., in press, 1978.
10. MacGregor, M. I., Block, A. J., et al.: Topics in clinical medicine. Serious complications and sudden death in the Pickwickian syndrome. Bull. Johns Hopkins Hosp., *126*:279, 1970.
11. Mancini, M., Contaldo, F., et al.: Frequency relevance and reversibility of medical complications of obesity. (abstract). International Symposium on Medical Complications of Obesity, Serono Symposia 12. Naples, 1978.
12. Montemagno, U.: Gynecological complications from obesity. Serono Symposia 23. Naples, 1978.
13. Peckham, C. H., and Christianson, R. E.: The relationship between prepregnancy weight and certain obstetric factors. Am. J. Obstet. Gynecol., *111*:1, 1971.
14. Prem, K. A., Mensheha, N. M., et al.: Operative treatment of adenocarcinoma of the endometrium in obese women. Am. J. Obstet. Gynecol., *92*:16, 1965.
15. Rabkin, S. W., Mathewson, F. A. L., et al.: Relation of body weight to development of ischemic heart disease in a cohort of young North American men after a 26 year observation period: The Manitoba Study. Am. J. Cardiol. *39*:452, 1977.
16. Rimm, A. A., Werner, L. H., et al.: Disease and obesity in 73,532 women. Obesity Bariatric Med., *1*:77–84, 1972.
17. Rooth, G., and Carlstrom, S.: Therapeutic fasting. Acta Med. Scand., *187*:455, 1970.
18. Seltzer, C. C.: Overweight and obesity. The associated cardiovascular risk. Minn. Med., *52*:1265, 1969.
19. Society of Actuaries: Build and blood pressure study. Chicago, Illinois, Society of Actuaries, 1959.

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Adipose Tissue Morphology and Morbid Obesity

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Selection of obese subjects for surgical intervention usually seems to be performed after several therapeutic attempts with conventional treatment have failed in those who suffer from very severe obesity. Contraindications in psyche and soma are then also taken into account. This is the safest way, but not only is this a negative type of selection, it also takes long periods of effort, and psychological, physical, and economic suffering before unconventional therapeutic measures such as surgery are considered. Although the current attitude toward surgery in obesity is still one of reluctance, and, at least from the point of view of the internist, something of a final capitulation, it would no doubt be valuable to have a tool for prediction of poor outcome of conventional treatment to add to other selection criteria.

Means to predict poor prognosis of treatment of obesity by diet have been sought in evaluation of age, sex, age at onset of obesity, severity of obesity, psychological factors, and so forth. In very rough terms it seems that a somewhat better prognosis is obtained in young men with late onset moderate obesity who are stable psychologically. A worse prognosis obtains in older women with severe obesity which began at a young age, and these women often seem to be labile psychologically. In addition to being based on widely overlapping results these conclusions often seem to be poorly defined insofar as prognosis is concerned. It may well be that prognosis for losing weight in absolute or relative terms is quite different from prognosis defined as the ability to maintain weight reduction after therapy.

Regulatory factors for maintenance of a certain mass of body fat located within adipose tissue itself have previously been suggested (the lipostat theory).[15] Such factors, if present, would theoretically inhibit attempts to decrease body fat. During recent years it has been possible to reexamine this concept in more precise terms, when the functional unit of adipose tissue, the adipocyte, has been defined in terms of degree of filling (adipocyte size) and total capacity (number of adipocytes). Furthermore, variations in both of these variables produce large changes in the total cellular surface area of adipose tissue, which has an important

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regulatory function for the degree of filling and emptying of adipose tissue because of the location of hormonal receptors and key enzymes on or in the vicinity of the surface of the adipocytes. The following article is a summary of recent research in this field.

Adipose Cellularity and Prognosis for Diet Treatment

Early studies indicated preliminarily that obese subjects with adipose tissue consisting of an increased number of fat cells would find it difficult to reduce.[3] In order to examine this potentially important question systematically, about 100 obese women were followed over several years under standardized conditions.[17] After initial measurements of body fat, average size of fat cells, and total number of fat cells, these women were subjected to low energy intake without anorectic drugs and with regular visits to the same doctor every third week. These conditions for treatment were similar to those of ordinary outpatient routines but were standardized as much as possible to allow analyses afterward.

In general the following expected events occurred. First, a decrease in body weight occurred, which sooner or later diminished to end eventually on a steady level. Significant effort was made to ensure that the patient followed the prescribed diet, and that the patient continued the three-week controls. A more rigorous diet was not advised in terms of diminishing energy intake further. After different periods of time, body weight again increased, and, once begun, in many patients, uncontrollable drastic overeating ensued. At this point, of course, many patients found it meaningless to continue visits, and here weight-records were registered by occasional weighings, telephone contacts, and so forth. Every effort was made to prevent overeating and to make the patient adhere to the prescribed diet.

When looking retrospectively at the diet histories obtained from the patients during the regaining phase, one is struck by the dramatic overeating in several patients. This gorging appears often to be triggered suddenly. Once surrendering the suffering of dieting because no further success is obtained, it may be that all inhibitions are released and a limitless gorging starts. Histories of caloric intakes of two to three times that needed might, however, suggest other than psychological mechanisms.

The weight records were analyzed afterward with definitions of the start of the steady state period and the regaining period at arbitrary norms. The following results were obtained in relation to adipose tissue morphology. Patients obese because of an increased number of adipocytes lost weight at a higher rate than patients obese because of enlargement of fat cells. They were also fatter from the outset, and never reached a body weight anywhere near the normal range. The period of weight maintenance was much shorter, and relapse occurred at a high rate. The whole cycle of decrease, weight maintenance, and relapse was finished earlier in the hyperplastic obese subjects.

These were the actual events in descriptive terms. It might be argued that this cycle had nothing to do with the adipocytes, and could have occurred simply because the hyperplastic obese subjects were much more obese. Perhaps they found it hopeless after some time to reach a weight any-

where close to normal weight, and therefore stopped treatment and relapsed. Statistical analyses argue against such an explanation. In multiple regression analyses, fat cell number was the main explanatory factor in comparison with, for example, body fat, body weight, and size of fat cells. Furthermore, matching patients for body fat comparisons still revealed significant associations between a short period of time of weight maintenance and a rapid rate of relapse, and hyperplastic obesity.

This study was recently repeated in patients who were treated in a hospital, with stricter restriction of energy intake, with the addition of exercise.[7] Patients were carefully instructed in how to continue therapy after having been discharged. Retrospective analyses of the same variables revealed a similar result: a relapse of patients with hyperplastic adipose tissue after a short period of time, and a very sad general picture with relapses of virtually all the patients within a few years.

Other Predictors for Prognosis

The basal metabolic rate has been found to be of value for predicting the rate of decrease in the initial treatment.[13, 18] This is logical in that the total decrease in weight is a result of the balance between intake and expenditure of energy. Patients responding to diet treatment with a saving of energy by a decrease in basal metabolic rate are more difficult to treat successfully.

Insulin stimulation by the sight of a meal (cephalic insulin stimulation) also seems to have some additional predictive power. Both basal metabolic rate and the insulin stimulation test are, however, of no value in predicting the duration of weight maintenance and the rate of relapse.[18]

Adipose Tissue and the Regulation of Energy Balance

These studies suggest that some regulatory factor prevents the further decrease of body fat below a certain limit possibly associated with the degree of filling of adipose tissue, that is, the amount of triglyceride in the fat cells which determines the size of adipocytes.[6] Further support for such a hypothesis is obtained from work in the experimental animal. Faust[11] and Kral[16] showed simultaneously that surgical removal of fat from rats did not produce a compensatory increase in the remaining fat, in either size or number of fat cells. This removal of fat did not change the size of the fat cells, but decreased their number. If, on the other hand, the fat store in the human body is diminished by a decrease in the size of fat cells by a negative caloric balance, then compensatory mechanisms tend to make up the deficiency, as demonstrated in the diet treatment trials. These observations indicate that adipocyte size is the factor regulated by diet.

Recent work from the Rockefeller group provides further support for this hypothesis.[12] Adult rats were given palatable food, causing overeating, obesity, and an increase in the number of fat cells. When these rats were given ordinary rat chow, they ate less and decreased in weight down to the same cell size as the controls eating ordinary rat chow the entire time. Since the experimental group now had more fat cells, they had a remaining obesity of a pure hyperplastic type. It was as if the size of the fat

cells was in some way associated with energy balance, probably by interfering with food intake.

What the messenger between adipose tissue expansion (fat cell size) and energy balance regulation might be is unknown, but some considerations might be pertinent. A product from adipocytes secreted in different quantities from small and large fat cells might be a messenger. Such products are glycerol and free fatty acids, which are produced at a higher rate in larger adipocytes because of their increased lipolytic rate.[5, 10, 24, 26] Free fatty acids are reesterified to a certain extent, depending on, among other things, the availability of glucose. Glycerol is, however, a metabolic end product of adipocytes, and would fit in nicely theoretically as a messenger either directly or through its transformation during gluconeogenic processes in the liver. Experimental tests of such a hypothesis have been performed, showing that the hypothalamus metabolizes glycerol at a higher rate than other parts of the brain.[14]

There are also other possibilities. Larger fat cells have an increased turnover of triglyceride in the hydrolysis-reesterification cycle.[5] This means that a waste of energy is occurring. The increased production of free fatty acids may also cause energy losses in another, wider, vicious circle through liver synthesis of very low density lipoproteins which are again taken up in adipose tissue. A diminution of fat cells by, for example, decreased energy intake would thus save energy, and therefore tend to maintain triglyceride in adipose tissue. It is questionable, however, whether these energy savings are of sufficient quantitative importance. They may contribute to the increasing difficulty of losing further weight at a given adipocyte size, but it is unlikely that they play a significant role in the weight gaining phase after reducing.

Other adipose tissue factors probably play a more important role. When a patient is ending a period of diet therapy and is beginning a weight-maintaining, isocaloric diet, this is actually a physiologic situation similar to that of starvation-refeeding. A number of observations pertain to energy storage in this situation, as well as in meal-feeding versus nibbling in the experimental animal. Adaptations occur in the liver as well as in adipose tissue, and are frequently more pronounced in the latter. These adaptations seem in teleological terms to be well suited to capture substrate effectively for storage in adipose tissue, and they include increases in the enzymic equipment for de novo fatty acid synthesis[21] as well as in the pathways providing hydrogen for this synthesis.[25] Furthermore, triglyceride synthesis,[1] lipoprotein lipase activity,[23] and insulin sensitivity[1] are increased. The effects are dependent on the time of refeeding[19] as well as the type of nutrient used for refeeding, where carbohydrate seems to show the largest effects.[20] Most of these studies have been performed in the experimental animal, but certain key observations have been made in man, demonstrating that fatty acid and triglyceride synthesis[1] as well as insulin sensitivity,[1] lipoprotein lipase activity,[23] and glycerophosphate shuttle enzymes[9] are all elevated.

A major difficulty for interpretation of the refeeding-fasting experiments in adipose tissue has been that the elevated activities measured usually have been expressed in terms of wet weight of adipose tissue.

The fasting period before the refeeding causes a decrease in the weight of the fat cells, and therefore an increased amount of active cellular protein per unit wet weight, simply because adipocyte triglyceride has been mobilized. Such an increased metabolic activity probably has little or no meaning from the biological point of view. However, it has been found that when compared on a per cell basis, glucose metabolic pathways do indeed show increased activity, including synthesis of fatty acid and probably pentose shunt enzymes.[8] Lipoprotein lipase activity is also increased.

This summary shows that adipose tissue in the fasting-refeeding situation adapts to an efficient capture of substrate for triglyceride storage. One might then ask whether this capture is so efficient that it has consequences for regulation of plasma energy substrate concentrations and, therefore, possibly for energy intake regulation. For an example, let us consider glucose. Lower blood glucose levels have been observed in fasting-refeeding rats which could not be explained by glucose uptake in adipose tissue which, although elevated in fasted-refed rats, was only a small part of total glucose uptake.[2] In man, glucose uptake in adipose tissue is apparently also small in the postabsorptive phase,[4] but has never been examined in the fasting-refeeding situation. Although a substantial increase is needed in the refed situation in comparison with the postabsorptive phase to be of significance, this possibility can by no means be rejected.

Another possibility is more directly associated with the cellularity of adipose tissue. Regulatory factors important for the rate of metabolic processes are situated at or close to the cell surface. This is particularly true of hormone receptors. It should not be overlooked, however, that the cytoplasm of the adipocyte is stretched over the triglyceride droplet, and therefore is also dependent on the surface area. As a consequence, a certain amount of triglyceride carried in a few large fat cells means a smaller surface area than the same amount in smaller fat cells. Thus in hyperplastic obesity there is a larger active surface area of adipocytes than in hypertrophic obesity at the same degree of obesity. The adipose tissue of a reduced hyperplastic obese subject with previous severe obesity and many fat cells will then have a very large surface area.

The most important anabolic hormone for adipose tissue is probably insulin. Insulin receptors increase in number on adipocytes during weight decrease,[22] while the fat cells are diminishing in size, and circulating plasma insulin concentration is low.

Adipose tissue of a reduced hyperplastic obese subject will have a large surface area with optimal hormone and substrate availability from a geometric point of view. Upon refeeding, when the patient ends a diet of negative energy balance and begins a weight-maintaining isocaloric diet, both circulating insulin and substrate concentrations increase. The capacity of adipose tissue for insulin binding should be very high in this situation. Furthermore, refeeding adaptation of enzymes for substrate storage in adipose tissue takes place. It is easy to imagine that adipose tissue in this situation effectively captures circulating substrate, and like a sponge tends to self-regulate its energy content back to larger fat

cells and more stored triglyceride. The effects of these phenomena on substrate fluxes in the body and potential effects on energy intake regulation might be significant and should be examined.

Measurement of Adipose Tissue Cellularity as a Means for Selection of Patients for Surgery

It has been observed repeatedly that hyperplastic obese patients are those who have the worst prognosis in ordinary conventional treatment with establishment of a negative energy balance. The poor prognosis is mainly observed as an inability to maintain the lower weight after weight reduction. Clearly, this is where research efforts should be placed in the future to improve the prognosis for treatment. Systematic studies of treatments such as exercise, group therapy, behavioral therapy, different diets during refeeding, and possibly drugs may modify the prognosis. Cellularity measurements of adipose tissue have, in our opinion, been helpful in focusing on this aspect of the problem.

Should adipocyte measurements be part of the basis on which indications for surgery are built? The methodology is fairly easy to set up. We have used it as one ingredient in the comparatively few patients operated on in Göteburg, but we do not find it to be indispensable. Enormous obesity, which probably still is the only instance in which surgery is performed, is almost always hyperplastic. Studies of adipose tissue morphology and function in this area are probably significant mainly as a research tool, helping to define and elucidate the mechanisms behind the rapid relapse of treated hyperplastic obesity.

REFERENCES

1. Björntorp, P., Scherstén, T., and Gottfries, A.: Effects of glucose infusions on adipose tissue lipogenesis in man. Acta Med. Scand., *183*:565, 1968.
2. Björntorp, P., Krotkiewski, M., Larsson, B., et al.: Effects of feeding states on lipid radioactivity in liver, muscle and adipose tissue after injection of labelled glucose in the rat. Acta Physiol. Scand., *80*:29, 1970.
3. Björntorp, P., Sjöström, L., Berchtold, P., et al.: Diagnose und Behanlung der Adipositas. Schweiz Rundschau. Med. (Praxis), *60*:698, 1971.
4. Björntorp, P., Berchtold, P., Holm, J., et al.: The glucose uptake of human adipose tissue in obesity. Europ. J. Clin. Invest., *1*:480, 1971.
5. Björntorp, P., and Sjöström, L.: The composition and metabolism in vitro of adipose tissue fat cells of different sizes. Europ. J. Clin. Invest., 2:78, 1972.
6. Björntorp, P., Carlgren, G., Isaksson, B., et al.: The effect of an energy-reduced dietary regimen in relation to adipose tissue cellularity in obese women. Am. J. Clin. Nutr., *28*:445, 1975.
7. Björntorp, P., Krotkiewski, M., Forestier, G., et al.: Adipose tissue morphology and obesity treatment. Prediction of weight maintenance after controlled treatment. Am. J. Clin. Nutr., in press, 1979.
8. Björntorp, P., Enzi, G., Karlsson, M., et al.: Fat cell metabolism after weight reduction. Int. J. Obesity, in press, 1979.
9. Bray, G. A.: Lipogenesis in human adipose tissue: Some effects of nibbling and gorging. J. Clin. Invest., *51*:537–548, 1972.
10. Faulhaber, J. D., Petruzzi, E. N., Eble, H., et al.: In vitro-Untersuchungen über den Fettstoffwechsel isolierter menschlicher Fettzellen in Abhängigkeit von der Zellgrösse: Die durch Adrenalin induzierte Lipolyse. Horm. Metab. Res., *1*:80, 1960.
11. Faust, I. M., Johnson, P. R., and Hirsch, J.: Noncompensation of adipose mass in partially lipectomized mice and rats. Am. J. Physiol., *231*:538–544, 1976.
12. Faust, I. M., Johnson, P. R., Stern, J. S., et al.: Diet-induced adipocyte number increase in adult rats: a new model of obesity. Am. J. Physiol., 235:E279–E286, 1978.

13. Garrow, J. S., Durrant, M. L., Mann, S., et al.: Factors determining weight loss in obese patients in a metabolic ward. Int. J. Obesity, 2:441–447, 1978.
14. Goodner, C. J., Ogilvie, J. T., and Koerker, D. T.: The metabolism of glycerol by hypothalamic and pituitary tissues in vitro in the rat. Proc. Soc. Exp. Biol. Med., *143*:616–622, 1973.
15. Kennedy, G. C.: The role of depot fat in the hypothalamic control of food intake in the rat. Proc. Royal Soc., *140*:578, 1953.
16. Kral, J. G.: Surgical reduction of adipose tissue in the male Sprague-Dawley rat. Am. J. Physiol. *231*:1090–1096, 1976.
17. Krotkiewski, M., Sjöström, L., Björntorp, P., et al.: Adipose tissue cellularity in relation to prognosis for weight reduction. Int. J. Obesity, *1*:395, 1977.
18. Krotkiewski, M., Bjurö, T., Garellick, G., et al.: Insulin elevation after cephalic stimulation, basal oxygen uptake and fat cell number as predictors for slimming. Submitted for publication, 1979.
19. Leveille, G. A., and Hanson, R. W.: Influence of periodicity of eating on adipose tissue metabolism in the rat. Canad. J. Physiol., *43*:857, 1965.
20. Leveille, G. A.: Adipose tissue metabolism: influence of periodicity of eating and diet composition. Fed. Proc., *29*:1294, 1970.
21. O'Hea, E. K., and Leveille, G. A.: Influence of fasting and refeeding on lipogenesis and enzymatic activity of pig adipose tissue. J. Nutr., *99*:345, 1969.
22. Olefsky, J.: Decreased insulin binding to adipocytes and circulating monocytes from obese subjects. J. Clin. Invest., *57*:1165–1172.
23. Schwartz, R. S., and Brunzell, J. D.: Increased adipose tissue lipoprotein lipase activity in moderately obese men after weight reduction. Lancet, *1*:1230–1231, 1978.
24. Smith, U.: Insulin responsiveness and lipid synthesis in human fat cells of different sizes: Effect of the incubation medium. Biochim. Biophys. Acta, *218*:417, 1970.
25. Tepperman, H. M., and Tepperman, J.: Adaptive hyperlipogenesis. Fed. Proc., *23*:73, 1964.
26. Zinder, O., Arad, R., and Shapiro, B.: Effect of cell size on the metabolism of isolated fat cells. Israel J. Med. Sci., *3*:787, 1967.

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An Overview of Therapy for Morbid Obesity

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Morbid obesity is traditionally treated differently from less severe forms of overweight. The implicit assumption is that special therapeutic modalities are needed to manage extremely obese patients, particularly since the modalities which have been used—surgery, starvation, drugs, very low calorie diets, or liquid formulas—all subject the patient to an increased risk. In order to justify these procedures, all of which are hazardous in varying degree, one must assume that the extremely obese patient is unlikely to respond to conservative measures and has substantially increased morbidity and mortality associated with obesity.

Disorders Associated with Obesity

Increased mortality in obese patients, mainly from coronary heart disease, has been documented in many studies.[17, 28, 30, 31, 34, 39, 47] Some authors show obesity to be an independent risk factor for heart disease,[17, 30] but others have suggested that the independent contribution of obesity to coronary heart disease in obesity is small. Indeed, when other risk factors such as hypertension, hyperlipidemia, insulin-independent diabetes, physical inactivity, and smoking are factored out, moderate obesity is thought by Keys to plan an insignificant role in the pathogenesis of premature coronary heart disease.[31, 39] This issue may be moot since, with the exception of smoking, obesity contributes to the development of these well-established risk factors.[11, 14, 29] Weight reduction will reduce the blood pressure, blood glucose, and often serum cholesterol in obese patients who have elevations of these parameters. Thus, intensive therapy of obesity is justified in hypertensive, diabetic, or hyperlipidemic obese individuals. However, such metabolic abnormalities, while associated with overweight, are not universal phenomena in obesity. Diabetes and hypertri-

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glyceridemia are related to enlargement of fat cells but apparently not to an increased number of normal sized fat cells.[6-9] Although both hyperplasia and hypertrophy of adipocytes are seen in massively obese persons, hypertrophy alone can be seen in many less obese individuals.[7, 42] Dangerous metabolic abnormalities can be easily detected at routine clinical evaluation, and may serve as a justification for drastic therapy.

In addition to the problems discussed above, obesity may cause severe impairments predominantly on the basis of enlarged body mass. These include mechanical problems ranging from marked loss of physical agility to severe degenerative joint disease or ligamentous injuries in certain weight-bearing joints. Potentially life-threatening problems such as alveolar hypoventilation,[16] congestive heart failure,[2] or nephrotic syndrome[51] are seen in massively obese individuals, and as a result of these conditions they are more susceptible to diseases such as pneumonia, other types of kidney disease, or the complications of surgery. Fatty livers are seen in many obese individuals,[41, 52] but severe functional hepatic impairment is rare. The above problems justify intervention on the basis of body mass alone, but in most centers a greater degree of overweight is required to justify the aggressive therapy of "uncomplicated" massive obesity than would be the case for patients with metabolic or serious clinical disturbances.

Conventional Therapy

The presence of massive obesity per se does not necessarily mean that conventional methods will fail to produce weight loss. Indeed, the absolute basal metabolic rate (in kcal per day) is higher in massively obese than in less obese patients (Fig. 1), and the energy output associated with standard physical activity is usually greater also. Thus, these patients expend more energy than the less obese individual, and can initially achieve weight reduction on higher food intakes. In general, more rapid weight loss has been seen in heavier patients in our program despite frequently greater calorie intakes (Fig. 2). In addition, a larger proportion of these patients have lost weight. We are currently treating in a

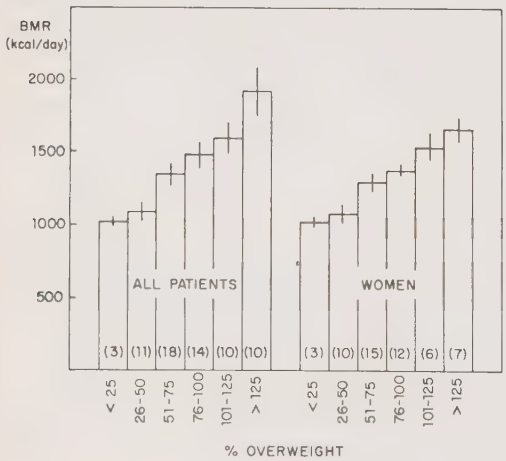

Figure 1. The basal metabolic rates in 66 consecutive obese patients are displayed as a function of their per cent above desirable body weight. The number of patients in each group is in parentheses. Values are mean ± 1 standard deviation.

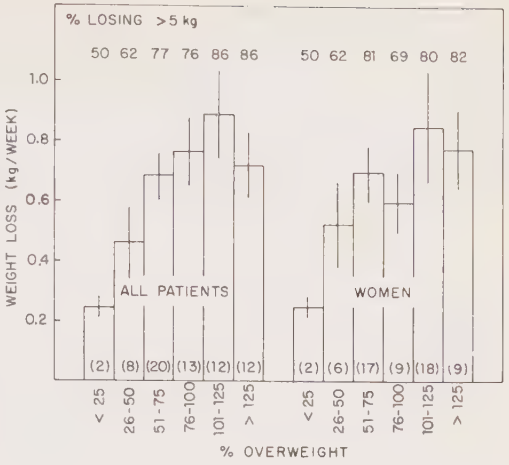

Figure 2. The rate of weight loss during the period of active weight reduction in 67 obese patients who lost at least 5 kg in a dietary and behavioral program is displayed as a function of the per cent over desirable body weight. The per cent of all entering patients in each weight class who lost at least 5 kg is shown at the top of the figure, and the number of patients is in parentheses. Values are mean ± 1 standard deviation.

behavioral group a woman who has lost 60 kg, from an initial weight of 203 kg, on a reported intake (by food intake diaries) of 1500 to 2000 kcal per day. Her mean weight loss is 1.28 kg per week. However, she demonstrates the main drawback to conservative therapy in massively obese patients. After 11 months, despite a mean rate of loss comparable to that achieved by bypass surgery, she is still 130 per cent above her "desirable" weight. Not surprisingly, many patients lack the patience to adhere to a diet for a year or more without either the reinforcement from more rapid weight loss or the mechanical block imposed by surgery.

Starvation and Very Low Calorie Diets

To hasten weight reduction, starvation and very low calorie formulas have been devised. Starvation has allowed weight loss at rates as high as 5.6 kg per week over a two-month period for a 250 kg patient.[14, 20] Complications of starvation regimens include severe postural hypotension, hyperuricemia, acidosis, transient hepatic and renal impairments, and loss of minerals. Supplementation with sodium, potassium, bicarbonate, and vitamin-mineral preparations is routine, as is the use of allopurinol. Patients must be hospitalized during prolonged fasting. Body protein loss (indicated by negative nitrogen balance) continues throughout the program. Nitrogen loss is 3 to 5 gm per day even after a month of fasting. It is evident that weight loss is accelerated by the excessive loss of lean body mass.

Because of the need for hospitalization during total fasting, very low calorie "supplemented fasts" have been introduced. The composition of these regimens varies, but most of them provide an intake of 400 kcal per day or less of food which can only be described as monotonous. It has been claimed that an intake of 1.5 gm of protein per kg of average desirable body weight as lean meat or fish with no carbohydrate will cause "protein sparing" and return the subject to nitrogen equilibrium or positive nitrogen balance.[22, 23] This has been ascribed in part to ketosis. However, similar protein-sparing effects have been demonstrated on a formula diet of 30 gm of protein and 45 gm of carbohydrate daily.[4] In contrast, in recent

studies by our group, nitrogen equilibrium was only transiently achieved on a formula intake of 1.5 gm of a high quality protein mixture per kg of desirable body weight per day. Equilibrium occurred after about four weeks of formula intake after which nitrogen balance again became intermittently negative. Thus, it is unlikely that any of these diets predictably spares protein, although protein loss clearly is lower than that during total fasting.

Apart from reducing the rate at which lean body mass is depleted, the major advantages of the very low calorie formulas over fasting have been improved exercise tolerance and the ability to employ these programs in an ambulatory setting. A large scale application of this approach has been conducted by Vertes and Genuth,[25, 50] who now have almost 1200 patient years of experience with only four deaths and minimal morbidity. The mortality rate is not greater, and probably less, than that which might be expected in an untreated group of morbidly obese patients over the same period. Control of diabetes and hypertension has been achieved in most of these patients. Side effects have generally been mild but have included orthostatic hypotension, dry skin, hair loss, constipation, cold intolerance, muscle cramps, easy fatigability, and halitosis.

A major problem with starvation or supplemented fasting regimens has been the high rate of recidivism after substantial weight loss has been achieved. Drenick has reported that 93 per cent of a group of patients who were hospitalized for starvation regimens regained their weight within nine years of reduction.[21] Similar high rates of weight regain have been seen on shorter follow-up in other studies. Thus, the expense and effort of weight reduction seem to be wasted in these patients if their excessive body fat is reaccumulated. It is for this reason that surgical therapy is often perceived as an attractive alternative.

"Liquid Protein" Diets

The "liquid protein" diet, as popularized by a best-selling book, was widely used in recent years with disastrous results. This diet was an adaptation of the supplemented fasts described above, but consisted of a very low quality protein (collagen hydrolysate) supplemented with tryptophan. Obese patients frequently used this preparation without appropriate vitamin and mineral supplementation and with little or no medical supervision. To date, almost 60 patients are known to have died while taking liquid protein or within two weeks of stopping its use.[49] A typical profile shows rapid weight loss of 10 to 60 kg over a period of two to eight months in previously healthy obese women. Deaths are preceded by prolongation of the QT interval and reduction of the QRS amplitude on electrocardiogram, followed by multiple ventricular arrhythmias which respond poorly to pharmacologic therapy. Hypokalemia and hypocalcemia are sometimes seen, but not invariably. At autopsy, myofiber atrophy with loss of myofibrillar delineation and, in one instance, myocarditis, have been seen. The cause of these changes is unknown, but protein malnutrition causes a similar picture in monkeys.[28] Another possibility is excessive mineral loss, including potassium, magnesium, phosphorus, or copper.[20] In addition to myocardial deaths, some patients have developed hemor-

rhagic pancreatitis on refeeding. It is not clear whether these hazards are peculiar to the collagen hydrolysates or whether they would be seen in other very low calorie programs if an equal number of patients were followed. Until the cause of myocardial deaths associated with supplemented fasting is clarified, the use of this form of therapy should be undertaken with proper restraint. Patients should be fully cognizant of the hazards involved, and should be followed closely by physicians who are experienced with these diets.

Ketogenic Diets

"Unbalanced" (usually ketogenic) diets have also been popular for treatment of all forms of obesity. As with starvation and supplemented fasting, the initial rate of weight reduction is rapid, and the patient is encouraged by this early success. However, subsequent weight loss is slower. In studies by our group in which the energy-nitrogen balance method was used to estimate composition of weight change, it was clear that the rapid weight loss that occurs at the onset of a ketogenic diet is caused by water diuresis.[53] The rate of fat loss was identical on balanced and ketogenic diets. The greater weight reduction in starvation was caused by nitrogen loss (Fig. 3), and by the greater caloric deficit. Indeed, it is likely that rapid weight reduction (that is, greater than 0.5 kg per day) which is sustained for more than a week is always associated with excessive protein loss, since depot fat is calorically dense. If this is true, then rapid weight loss on any regimen, if sufficiently prolonged, may cause a form of protein-calorie malnutrition. As mentioned above, heart disease pathologically similar to that seen in the "liquid protein" deaths can be seen in experimental protein-calorie malnutrition.[18] Thus, it is possible that too rapid weight loss from any cause may increase the risk of cardiac deaths.

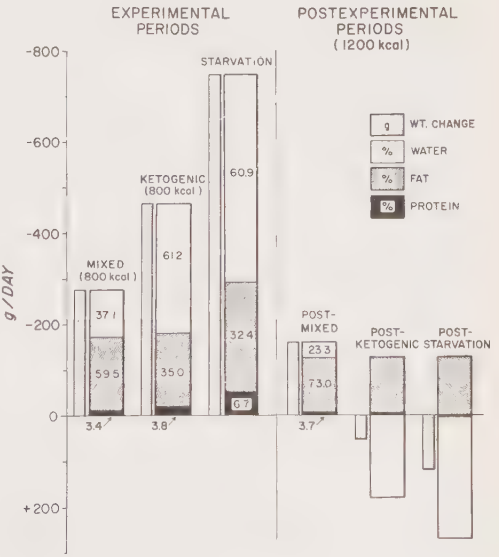

Figure 3. Quantity and composition of weight lost by six obese men on starvation, mixed 800 kcal, and ketogenic 800 kcal diets are shown. (*From* Yang, M-U and Van Itallie, T. B.: Composition of weight lost during short-term weight reduction: Metabolic responses of obese subjects to starvation and low-calorie ketogenic and nonketogenic diets. J. Clin. Invest., 58:722, 1976, with permission.)

Surgical Treatment

The surgical procedures used to treat morbid obesity will be described in great detail in other papers in this symposium. They fall generally into intestinal bypass procedures, initially designed to produce malabsorption, and gastric procedures, overtly designed to reduce food intake by limiting the reservoir capacity of the stomach. In point of fact, reduced food intake is also seen in intestinal bypass procedures in man[13, 40] and in rats,[32] and it appears to be the major factor causing weight loss in patients who undergo the jejunoileal bypass operation.

In our program, intestinal bypass surgery has been abandoned because of the frequent serious side effects associated with the procedure. Prospective studies have indicated that the morbidity of the gastric bypass procedures during the first year is far less than for jejunoileal bypass, although both operations induce similar rates of weight loss.[1, 27] However, the gastric bypass is a relatively new procedure, and long-term complications are unknown. Jejunoileal bypasses have been associated with deaths from end-stage cirrhosis,[23, 36, 46] and with many severe complications including arthritis,[44] calcium oxalate kidney stones,[26, 38] intestinal bacterial overgrowth,[5, 22, 24] proctitis, and cholelithiasis.[12] Chronic nutrient losses have resulted in symptomatic hypocalcemia,[19, 43] hypokalemia,[43] and hypomagnesemia.[33] Vitamins, including parenteral B_{12}, are usually prescribed but patient compliance during follow-up is often low. Low levels of serum 25-hydroxycholecalciferol have been seen,[48] and thus osteomalacia can be a late complication in these patients. It has been postulated that hepatic failure may be caused by bacterial overgrowth in the bypassed segment of bowel,[15] or may be a result of malabsorption of amino acids.[37] Thus, use of antibiotics or perfusion of the excluded segment with saline, amino acids, or other nutrients via an externalized catheter at the proximal end might reduce complications. However, the gastric procedures entirely eliminate these particular problems. Thus, the main advantage of intestinal bypass appears to be that this procedure is technically less demanding than gastric surgery. This may make jejunoileal bypass preferable, at least on a temporary basis, in patients who are exceptionally poor surgical risks.

Gastric procedures can be classified into those which bypass the duodenum (gastric bypass) and those which employ the normal anatomic route (gastroplasty). The latter is theoretically preferable because it should allow better absorption of iron and vitamin B_{12}, and permit mixing of gastric contents with bile and pancreatic secretions. Gastric acid secretion should be greater with the gastroplasty because the antrum is intact, which could lead to ulcer disease or reflux esophagitis. In addition, the size of the outlet from the fundic pouch may be less easily controlled in the gastroplasty, so success would be less predictable.

Regardless of the specific type of procedure, a successful gastric operation causes weight loss by forcing the patient to eat small meals. It is possible to outeat the bypass with frequent small ingestions, especially liquids. Patients who try to eat large meals develop a sense of fullness followed by vomiting or esophageal reflux. Undoubtedly, the discomfort produces aversive conditioning. Despite the side effects that may occur,

patients who have had gastric surgery,[35] and those who have had intestinal bypass,[15] are generally pleased with the results of surgery.

Flexible Approach to Treatment

In light of the foregoing discussion, our group has adopted a flexible approach to the treatment of morbidly obese patients. We prefer to have all patients begin in a basic calorie management program, in which they are given a target calorie intake (derived from basal metabolic rate and estimates of physical activity) and are aided in achieving this goal through behavioral and nutritional tools. Those patients with severe disabilities caused by obesity, in the categories described at the beginning of this paper, are carefully considered for transfer to an alternative therapeutic program. If the patient fails to comply with the initial program, frequently manifested by poor attendance, or to lose weight at a rate of at least 1 kg per week, we discuss with the patient the options of supplemented fasting using a 400 kcal formula or of gastric surgery. It is imperative for the patient to have detailed knowledge of possible complications associated with drastic food restriction or gastric surgery. Patients who enter a supplemented fasting program frequently continue to attend group sessions with patients on food-oriented diets. It is hoped that their initial training and their continued contact with other patients and therapists will help them to be weaned to food for subsequent weight loss or maintenance or both. Surgical patients are also encouraged to remain in groups. Follow-up evaluation of formula and bypass patients during rapid weight loss is shown in Tables 1 and 2. We feel that the extensive follow-up is warranted in both groups because of the possibly hazardous effects of rapid weight loss independent of the means of achieving it. Close surveillance of the food intake of the surgical patient is required because they may select an imbalanced intake. Vitamin and mineral replacement are essential.

Some patients come to us with a need to lose a specified amount of weight rapidly. This is particularly true for those who urgently require a surgical procedure (such as an orthopedic operation) which cannot be done because of the obesity. In these cases, the patients are given a course of supplemented fasting, with the expectation that they will enter a comprehensive program of calorie management after surgery.

A different problem is posed by patients who present or are referred

Table 1. *Follow-up Evaluation of Patients on Very Low Calorie Formulas*

Every week:	Upright and recumbent pulse and blood pressure Rhythm strip (leads II and AVL) Urine sugar and acetone
Every two weeks:	Blood glucose, urea, electrolytes, uric acid, lactate, β-hydroxybutyrate, acetoacetate, 24-hour urine sodium, potassium, magnesium, manganese, zinc, copper, and nitrogen
Every month:	Complete blood count, hepatic enzymes, calcium, phosphorus, magnesium, protein electrophoresis, and lipids Full electrocardiogram

Table 2. *Follow-up Evaluation of Patients After Gastric Bypass*

Every week:	Urine sugar and acetone
Every two weeks:	Glucose, urea, and electrolytes
Every month:	Complete blood count, hepatic enzymes, calcium, phosphorus, iron, folate and B_{12}, and lipids Electrocardiogram

solely for bypass surgery. In these cases, the initial evaluation includes extensive discussion of the risks and side effects of surgery and how the patient's daily habits of food intake will change. Psychiatric consultation is frequently helpful in clarifying the issues for the patient and the physician.

SUMMARY

There are a variety of therapeutic approaches to morbid obesity, all of which suffer to some extent from lack of efficacy, including possible recidivism and potential complications which may be extremely serious. In general, it is best to try the most conservative techniques first, but to recognize that this is a group of patients in whom the risks of drastic treatment, including intestinal surgery, may be more than balanced by the disadvantages and hazards posed by an incapacitating burden of stored fat.

REFERENCES

1. Alden, J. F.: Gastric and jejunoileal bypass. A comparison in the treatment of morbid obesity. Arch. Surg., *112*:799, 1977.
2. Alexander, J. K.: Effects of weight reduction on the cardiovascular system. *In* Bray, G. F., et al. (eds.): Obesity in Perspective. Washington, D.C., U.S. Government Printing Office, 1973, pp. 233–238.
3. Apfelbaum, M., Boudon, P., Lacatis, D., et al.: Effets metaboliques de la diete protidique chez 41 sujets obeses. Presse Med., 78:1917, 1970.
4. Baird, I. M., Parsons, R. L., and Howard, A. N.: Clinical and metabolic studies of chemically defined diets in the management of obesity. Metabolism, 23:645, 1974.
5. Barry, R. E., Benfield, J. R., Nuell, P., et al.: Colonic pseudo-obstruction: A new complication of jejunoileal bypass. Gut, *16*:903, 1975.
6. Bernstein, R. S., Grant, N., and Kipnis, D. M.: Hyperinsulinemia and enlarged adipocytes in patients with endogenous hyperlipoproteinemia without obesity or diabetes mellitus. Diabetes, 24:207, 1975.
7. Björntorp, P., and Sjostrom, L.: Number and size of adipose tissue fat cells in relation to metabolism in human obesity. Metabolism, 20:703, 1971.
8. Björntorp, P., Gustafson, A., and Persson, B.: Adipose tissue fat cell size and number in relation to metabolism in endogenous hypertriglyceridemia. Acta Med. Scand., *190*:363, 1971.
9. Björntorp, P., Jonsson, A., and Berchtold, P.: Adipose tissue cellularity in maturity onset diabetes mellitus. Acta Med. Scand., *191*:129, 1972.
10. Blackburn, G. L., Bistrian, B. R., Flatt, J. P., et al.: Role of a protein sparing modified fast in a comprehensive weight reduction program. *In* Howard, A. (ed.): Recent Advances in Obesity Research. London, Newman Publishing, 1975, pp. 279–281.
11. Bortz, W. M.: Metabolic consequences of obesity. Ann. Intern. Med., *71*:833, 1969.

12. Bray, G. A.: Intestinal bypass surgery for obese patients. Behavioral and metabolic considerations. Psych. Clin North Am., *1*:673, 1978.
13. Bray, G. A., Barry, R. E., Benfield, J. R., et al.: Intestinal bypass surgery for obesity decreases food intake and taste preferences. Am. J. Clin. Nutr., *29*:779, 1976.
14. Bray, G. A., Davidson, M. B., and Drenick, E. J.: Obesity: A serious symptom. Ann. Intern. Med., *77*:779, 1972.
15. Bray, G. A., Granway, F. L., Barry, R. E., et al.: Surgical treatment of obesity. A review of our experience and an analysis of published reports. Int. J. Obesity, *1*:331, 1977.
16. Buskirk, E. R., and Bartlett, H. L.: Obesity and pulmonary function. *In* Bray, G. F., et al.: Obesity in Perspective. Washington, D.C., U.S. Government Printing Office, 1973, pp. 225–231.
17. Chapman, J. M., Coulson, A. H., Clack, V. A., et al.: The differential effect of serum cholesterol, blood pressure and weight on the incidence of myocardial infarction and angina pectoris. J. Chron. Dis. *23*:631, 1971.
18. Chauhan, S., Nayek, N. S., and Ramalingaswami, V.: The heart and skeletal muscle in experimental protein malnutrition in rhesus monkeys. J. Pathol. Bacteriol., *90*:301, 1965.
19. Demuth, W. E., and Rottenstein, H. S.: Death associated with hypocalcemia after small-bowel short circuiting. New Engl. J. Med., *270*:1239, 1964.
20. Drenick, E. J.: Weight reduction by prolonged fasting. *In* Bray, G. A., et al.: Obesity in Perspective. Washington, D.C., U.S. Government Printing Office, 1973, pp. 341–360.
21. Drenick, E. J., and Johnson, D.: Weight reduction by fasting and semistarvation in morbid obesity: Long-term follow-up. Int. J. Obes., *2*:123, 1978.
22. Drenick, E. J., Ament, M. E., Finegold, S. M., et al.: Bypass enteropathy: An inflammatory process in the excluded segment with systemic complications. Am. J. Clin. Nutr., *30*:76, 1977.
23. Drenick, E. J., Simmons, F., and Murphy, J. F.: Hepatic morphology after treatment of obesity by fasting, diet and bowel bypass. New Engl. J. Med., *282*:829, 1970.
24. Feinberg, S. B., Schwartz, M. Z., Clifford S., et al.: Significance of pneumocystis cystoides intestinalis after jejunoileal bypass. Am. J. Surg., *133*:149, 1977.
25. Genuth, S. M., Castro, J. H., and Vertes, V.: Weight reduction in obesity by outpatient semistarvation. J.A.M.A., *230*:987, 1974.
26. Gregory, J. G., Starkloff, E. B., Miyai, K., et al.: Urologic complications of ileal bypass operation for morbid obesity. J. Urol., *113*:521, 1975.
27. Griffen, W. O., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedure for morbid obesity. Ann. Surg., *186*:500, 1977.
28. Hutchinson, J. J.: Clinical implications of extensive actuarial study of build and blood pressure. Ann. Intern. Med., *54*:90, 1961.
29. Kannel, W. B., Brand, N., Skinner, J. J., et al.: The relation of adiposity to blood pressure and development of hypertension. The Framingham study. Ann. Intern. Med., *67*:48, 1967.
30. Kannel, W. B., LeBauer, J. T., Dawber, T. R., et al.: Relation of body weight to development of coronary heart disease. Circulation *35*:734, 1967.
31. Keys, A., Aravanis, C., Blackburn, H., et al.: Coronary heart disease: Overweight and obesity as risk factors. Ann. Intern. Med., *77*:15, 1972.
32. Kissileff, H. R., Nakashima, R. K., and Stunkard, A. J.: Ileal bypass reduces food intake and increases intermeal interval in rats. Second International Congress on Obesity, 1977, p. 23.
33. Lipner, R.: Symptomatic magnesium deficiency after small intestinal bypass for obesity. Intern. Med. J., *1*:148, 1977.
34. Marks, H. H.: Influence of obesity on morbidity and mortality. Bull. N. Y. Acad. Med., *36*:296, 1960.
35. Mason, E. E., Printen, K. J., Blommers, T. J., et al.: Gastric bypass for obesity after ten years' experience. Int. J. Obesity, *2*:197, 1978.
36. McGill, D. B., Humphreys, S. R., Baggenstoss, A. H., et al.: Cirrhosis and death after jejunoileal shunt. Gastroenterology, *63*:872, 1972.
37. Moxley, R. T., Pozefsky, T., and Lockwood, D. H.: Protein nutrition and liver disease after jejunoileal bypass for morbid obesity. New Engl. J. Med., *290*:921, 1974.
38. O'Leary, J. P., Thomas, W. C., and Woodward, E. R.: Urinary tract stone after small bowel bypass for obesity. Am. J. Surg., *127*:142, 1974.
39. Peffenbarger, R. S., Wolf, P. A., Notkin, J., et al.: Chronic disease in former college students. I. Early precursors of fatal coronary heart disease. Am. J. Epidemiol., *83*:314, 1966.
40. Rodin, J., Moskowitz, H. R., and Bray, G. A.: Relationship between obesity and weight loss and taste responsiveness. Physiol. Behav., *17*:591, 1976.
41. Rozental, P., Biava, C., Spencer, H., et al.: Liver morphology and function tests in obesity and during total starvation. Am. J. Dig. Dis., *12*:198, 1967.

42. Salans, L. B., Cushman, S. W., and Weissman, R. E.: Studies on human adipose tissue. Adipose cell size and number in non-obese and obese patients. J. Clin. Invest., 52:929, 1973.
43. Salmon, P. A. The results of small intestinal bypass operations for the treatment of obesity. Surg. Gynecol. Obstet., *132*:965, 1971.
44. Shagrin, J. W., Frame, B., and Duncan, H.: Polyarthritis in obese patients with intestinal bypass. Ann. Intern. Med., 75:377, 1971.
45. Solow, C., Silverfarb, P. M., and Swift, K.: Psychosocial effects of intestinal bypass surgery for severe obesity. New Engl. J. Med., *290*:300, 1974.
46. Spin, F. P., and Weismann, R. E.: Death from hepatic failure after jejunoileal anastomosis. Am. J. Surg., *130*:88, 1975.
47. Stanley, J., Lindberg, H. A., Berkson, D. M., et al.: Prevalence and incidence of coronary heart disease in strata of the labor force of a Chicago industrial corporation. J. Chron. Dis., *11*:405, 1960.
48. Teitelbaum, S. L., Halverson, J. D., Bates, M., et al.: Abnormalities of circulating 25-OH vitamin D after jejunoileal bypass for obesity. Evidence for an adaptive response. Ann. Intern. Med., *86*:289, 1979.
49. Van Itallie, T. B.: Liquid protein mayhem. J.A.M.A., *240*:144, 1978.
50. Vertes, V., Genuth, S. M., and Hazelton, I. M.: Supplemental fasting as a large-scale outpatient program. J.A.M.A., 238:2151, 1977.
51. Weisinger, J. R., Kempson, R. L., Eldridge, F. L., et al.: The nephrotic syndrome: A complication of massive obesity. Ann. Intern. Med., *81*:440, 1974.
52. Westwater, J. O., and Fainer, D.: Liver impairment in the obese. Gastroenterology, 34:686, 1968.
53. Yang, M-U, and Van Itallie, T. B.: Composition of weight lost during short-term weight reduction: Metabolic responses of obese subjects to starvation and low-calorie ketogenic and nonketogenic diets. J. Clin. Invest., 58:722, 1976.

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Childhood Obesity

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Obesity appears to be an epidemic problem facing the physician today as evidenced by its incidence doubling in the past 75 years.[58] Thirty per cent of men and 40 per cent of women in the fifth decade are considered to be obese (greater than 20 per cent over ideal weight).[41] Although higher prevalence can be demonstrated with decreasing socioeconomic status,[24] within certain ethnic groups,[54] and so on, obesity does not spare any age group, socioeconomic class, or ethnic group. Thus infants, children, and adolescents are not to be excluded. Indeed, it has been estimated that at least 25 per cent of all children are obese.[1, 32] Unfortunately, obesity in children has not been recognized or accepted as a problem until recently. In part, this change in attitude is the result of recent reports suggesting that adult obesity has its origin in infancy or childhood. Several authors have shown that 75 to 80 per cent of obese children tend to become obese adults.[2, 38] Recent work on the determinants of cellularity in adipose tissue may suggest an explanation for this phenomenon.[10, 31] No longer can we consider childhood obesity to be something that children will "outgrow," but it may well be indicative of a life-long affliction. The relevance for investigation, prevention, and treatment of childhood obesity becomes obvious. Considerable controversy surrounds interpretation of available data, so that widely accepted programs of treatment or prevention are not yet a reality. This discussion focuses on the definition, prevalence, etiology, treatment, and prevention of childhood obesity.

DEFINITION

Obesity in the adult population has usually been defined by utilizing life insurance data for ideal weight. Similar data are not as readily available for children. One can simply define obesity as the presence of excessive body fat; however, attempting to define the criteria for excessive body fat is complicated. Total body fat can be measured but the methods are cumbersome and thus, for population studies, impractical. Two simple and convenient measurements of body fat are total body weight

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and skinfold thickness. Total body weight alone is of little value in the pediatric population because other variables such as age, height, sex, and body build should be considered. Several mathematical formulas have been described utilizing some of these variables. Shukla et al. employed a percentage weight for height ratio.[51] This formula, however, makes the tall child appear to be overweight and the short child appear to be underweight. A second index initially described by Eid used percentage weight at the age when height was at the 50th percentile.[17] In both formulas values greater than 120 are indicative of obesity; values between 110 and 120 indicate overweight; values from 90 to 120 are normal; and values less than 90 indicate underweight. Other investigators have used established weights for age and classify those infants greater than the 97th percentile as obese. Perhaps the best anthropometric measure of obesity is by determination of skinfold thickness; the triceps and subscapular areas are commonly measured. The standards for these measurements have been published by Tanner and Whitehouse,[56] and Shukla et al.[51] Despite the lack of universal agreement on criteria for defining obesity in infancy and childhood, considerable data exist from which some conclusions can be made.

PREVALENCE

It was estimated in a 1956 report by Johnson et al. that 12 per cent of prepubertal children and 16 per cent of adolescents were obese.[32] In a study reported in 1974 the incidence of obesity in children between three and five years of age was 13 per cent.[23] In Shukla's original paper (using percentage weight for height), 17.2 per cent of infants were obese and an additional 25.1 per cent were overweight.[51] Using the same data base but employing Eid's index (percentage weight at the age when height is at the 50th percentile), these values were 13.8 per cent and 25.6 per cent respectively.[17] In another study Taitz reported that 46 of 114 six week old infants (40 per cent) were above the 90th percentile for weight.[55] The prevalence of obesity may vary among countries as demonstrated by a study of Swiss children which showed that only approximately 3.6 per cent of seven year old children and 5 per cent of 10 and 15 year old children were obese (weight greater than 20 per cent above normal range).[25]

ETIOLOGY

The etiology of obesity has been the subject of an enormous effort in clinical and basic science research. The simple explanation of an imbalance of caloric intake as compared with caloric utilization, although true, probably does not fully explain the metabolic events occurring in the obese child. When investigating the etiology of obesity, it is necessary to consider the adipose "organ," metabolic alterations, psychological, environmental, and socioeconomic factors, and obesity syndromes.

Adipose Organ

The primary functions of adipose tissue are the formation, storage, and supply of fatty acids. Fat cells are one of the last specific cell types to develop.[29] During the third to fourth months of gestation, adipose cells can be identified around blood vessels in the subcutaneous tissue. These cells then rapidly accumulate fat. At birth, the adipose organ comprises 28 per cent of the total body weight. By one year of age when the infant's weight is three times the birth weight, the adipose organ weighs 20 per cent of the body weight but in actual mass has increased six times. Until recently little was known about the mechanisms governing the size of the adipose organ. One of the more startling discoveries in the past decade is that excessive caloric intake, or hypernutrition, during certain critical periods in infancy leads to an increase in the adipose organ.[9] This can be demonstrated by an increase in size of fat cells (hypertrophy) and also by an increase in the number of fat cells (hyperplasia).[31] It is then speculated that excess nutrition might "program" an infant to a lifetime problem of obesity.

In normal children the average adipocyte size increases during the first year of life and then remains constant.[31] Adipocyte size has been shown to correlate with skinfold thickness[6] but not with age.[18] In obese children fat cells are significantly larger than those of normal controls.[35] Number of adipose cells in normal children appears to be related to age.[21] Data from a study by Brook suggest that the period from the 30th week of gestation through the first year of life is particularly critical in influencing multiplication of fat cells.[8] This phenomenon is thought to occur also in obese children nine through 11 years of age.[16] Thus, the earlier the onset of obesity, the greater the hypercellularity.[8] It has been estimated that 80 per cent of obese children are of the hyperplastic type.[6] In obese children who have substained a significant weight loss there is a significant reduction in size but not in number of fat cells.[9] The number of adipocytes remain fixed after puberty, although the absolute number varies among individuals.[9]

Metabolic Alterations

With the complexity of interrelationships involved in the study of weight, several metabolic or hormonal aberrations could lead, or predispose, to obesity. An obvious question to pursue is what the relationship of adipocyte size and number is to hormonal variations. Conflicting data are available. Fasting insulin levels do not correlate with mean adipocyte weight but do correlate with adipocyte number.[16] Many studies of obese patients have shown a progressive loss of feedback for eating control. Fasting insulin levels rise progressively with increasing degrees of obesity, growth hormone response becomes blunted, and the sensation of satiety appears to be progressively less well perceived.[44] The disordered carbohydrate metabolism and hyperinsulinemia often occur in the absence of other clinical manifestations of diabetes mellitus. The abnormal oral glucose tolerance tests in these patients can be divided into monophasic and biphasic responses representing two distinct groups.[37] The significance of this finding is unclear.

Insulin receptors on fat cells have been used to study insulin resistance in human obesity. It has been shown that the concentration of insulin receptors is markedly decreased in obese patients with insulin resistance.[5] A decrease in the concentration of receptors will lead to a reduction in the absolute number of hormone receptor complexes formed. Provided that the steps distal to the receptors are normal, a shift to the right of the metabolic dose-response curve will occur (that is, diminished sensitivity). Therefore, greater concentrations of insulin will be required to achieve a given metabolic effect.[5] These changes, however, are reversible following weight loss.[5]

Fine control of triglyceride homeostasis by lipase may be altered in association with insulin insensitivity. Insulin has been shown to be an inhibitor of triglyceride lipase at much lower levels than are necessary to produce glucose transport.[22] A small alteration in control causing a 0.1 per cent excess per day of tryglyceride accumulation would result in a 30 per cent increase in fat storage in one year.[52]

Low plasma growth hormone levels have been associated with obesity, as well as blunted responses to various standard stimuli.[12] However, this phenomenon is partially reversible by reduction of adipose tissue mass.[34]

Increased adrenal cortical function, specifically in the reticular zone, has been demonstrated in obesity.[42] Conflicting data exist concerning the in vivo fatty acid response to exogenous epinephrine. Some investigators have demonstrated a decreased response to epinephrine and have suggested that the decreased fatty acid response may be a stimulus for the development of new adipose cells.[35]

The role of the central nervous system in obesity must not be overlooked. Animal studies suggest that there are two centers in the hypothalamus specifically related to hunger and satiety.[30] The ventral lateral nucleus responds to low blood glucose, initiating those signals leading to the sensation of hunger. The ventral lateral nucleus contains material which stimulates insulin secretion in vitro and in vivo.[52] The ventral medial nucleus initiates a sequence of impulses which is interpreted as satiety. This center responds to increased blood glucose in the presence of insulin.[39] Inter-nuclear neural connections serve to carry impulses from the stimulated nucleus which in turn inhibits the activity of the other nucleus. The Zucker rat serves as a good animal model for testing this hypothesis. This rat is reported to have a congenital hypothalamic lesion resulting in lack of satiety, thus leading to overeating and obesity. More recently, evidence has indicated that branched chain amino acids may also play a role in modulating appetite through a central nervous system mechanism which is located in the medial amygdala.[48]

Influence of Environment

In a previous section it was noted that numbers of adipose cells may be increased by overeating at critical periods during infant and child development. This effect can be presumed to be an environmental influence but its significance is as yet undetermined.

The effect of environment may actually precede gestation. Udall et al.[37] showed that prepregnant weight for height, and weight gain during pregnancy were associated with increased subcutaneous fat, as measured by skinfold thickness, in the neonate. Possible explanations for this finding include increased placental transfer of free fatty acids, decreased metabolic rate, and decreased physical activity in utero.

The relationship between obesity in the first year of life and subsequent obesity is unclear. In a series of 300 children evaluated in infancy, 17.2 per cent were considered to be obese; however, when 203 of these children were reevaluated at four to six years of age only 6.9 per cent were obese.[43] Mellbin and Vuille compared physical development at age seven years to infantile weight gain by using height increase from zero to seven years and weight for height at seven years as the dependent variables, and a variety of weight gain periods in infancy as the independent variables. They concluded that weight gain in the first year of life, or any fraction of the first year, was not a strong predictor of obesity at seven years of age. Asher reviewed the onset of obesity in children from two obesity clinics and noted that only 44 per cent were stated to have been obese since infancy.[1] However, Charney et al.[13] reviewed the weights of 366 infants born between 1945 and 1955 and compared them to their weights as adults. Infants who were above the 90th percentile during the first six months of life had a 2.5-fold greater chance of being greater than 10 per cent overweight than infants at the 50th percentile.

In a recent extensive study, Dine et al. showed that there were statistically significant relationships between height and weight at age five years and the same measurements at six months and birth.[15] However, approximately 70 per cent of variance at age five was not accounted for by measurement of weight in the first year of life. This author also did not find a difference in weight at five years of age between breast-fed and bottle-fed infants. Although bottle feeding was once thought to be one of the primary reasons for obesity in infants,[35] other investigators have not supported this hypothesis.[17, 40]

To test the converse of the hypothesis that excessive caloric exposure in utero or in infancy leads to persistent obesity (that is, hypocaloric exposure results in lower obesity rates), Ravelli et al. reviewed the records of a large number of 19 year old men who were exposed in utero to the Dutch famine of 1944 to 1945.[46] When exposure occurred during the last trimester of pregnancy, the prevalence of obesity 19 years later was significantly reduced. However, it was noted that if exposure involved the first and second trimesters, the prevalence of obesity was higher. The authors suggested that the period of intrauterine life when famine occurred might have been critical for hypothalamic differentiation, thus affecting the hunger and satiety centers.

The Ten State Nutrition Survey identified additional "environmental" trends.[21] Females were fatter than males at all ages; adolescence was a period of increasing fatness in the female, whereas there was a transient decrease of fatness in the male; the higher the socioeconomic status of children (both male and female), the greater the amount of adipose tissue; and white children were more fat than black children.

Genetic Determinants

The existence of genetic factors in the development of obesity has been clearly established only in animals. In man the problem is more complex because data are based on parent-child pairs, and twins and siblings, and often cannot effectively differentiate environmental-genetic interactions. Family studies indicate that if one parent is obese, 40 to 50 per cent of the children will become obese; if both parents are obese, 70 to 80 per cent of the children will be obese.[3, 49] Studies on twins have shown that identical twins reared in the same environment have less differences in weight than do fraternal twins.[35] However, when identical twins are reared in different homes, the weight differences increase but are still less than those found in fraternal twins.[35] Although these data suggest a genetic basis for obesity, the fact that overnutrition can affect fat cellularity and that birth weight does not correlate with adult weight suggests a nongenetic origin. Thus because of the complexity of the analysis, it is unlikely that a genetic basis for obesity will be demonstrated until a familial biochemical error is identified as resulting in the various abnormalities found in obese patients.

Psychological Aspects

As with other facets of obesity, the literature on the psychological aspects is extensive. Poor self-esteem and personality disorders are associated with abnormal dietary habits and decreased physical activity;[11, 36] however, it is difficult, if not impossible, to determine whether the psychological problems are the cause or the result of the obese state. It is probable that psychological abnormalities play a more dominant role in some patients.

Childhood Obesity Syndromes

PRADER-WILLI SYNDROME (HHHO SYNDROME). This syndrome is characterized by hypotonia, hypomentia, hypogonadism, and obesity. It is suspected that patients have a hypothalamic defect. Other features include short stature, microcephaly, and a characteristic facies. Obesity becomes apparent in the first decade of life and is extremely refractory to treatment.

LAURENCE-MOON-BIEDL SYNDROME. The principal findings include obesity, mental deficiency, polydactyly and/or syndactyly, retinitis pigmentosa, hypogonadism, chronic glomerulonephritis, nerve deafness, short stature, and diabetes insipidus. Inheritance is autosomal recessive with considerable variability of expression.

KLINEFELTER SYNDROME. The spectrum of manifestations is very broad and ranges from the male with eunuchoidal habitus, minimal androgenization, tiny firm testes, and quite abnormal psychopathic behavior to the individual who appears to be well masculinized, has no behavioral disorders, but who has small gonads. The genetic abnormality is that of 47, XXY karyotype. Plasma gonadotropins, especially FSH, are elevated and plasma testosterone is low to low normal. This syndrome is occasionally associated with marked obesity.

A multitude of other syndromes are associated with obesity and include Turner's syndrome, Alstrome-Hallgren syndrome, Morgagni syndrome, and triglyceride storage disease.[7] In addition, hormonal imbalances can lead to marked obesity. Cushing's disease, hypothyroidism, growth hormone deficiency, and Stein-Leventhal syndrome are only a few of the many endocrine abnormalites associated with obesity.

TREATMENT

The primary criteria for any method of management include effectiveness, sustained result, minimal side effects, and ease of administration. In children a criterion equally as important is maintenance, or increase, in lean body mass and continued linear growth. The Committee on Nutrition of the American Academy of Pediatrics statement in 1967 that "no treatment program has achieved more than minor success" is probably still applicable today.[11] Three basic requirements to achieve weight reduction are motivation, increased activity, and decreased caloric intake. While there is a lack of agreement on the relative importance of each of these requirements, the greatest controversy focuses on who should be treated. At what age should children be subjected to treatment? What level of obesity warrants intervention? How aggressive should the physician be in treating an obese child? Precise answers to these questions are not readily available. Despite the lack of agreement on who should be treated, several approaches have been utilized in the management of obesity in childhood, including dietary treatment, drug treatment, psychotherapy, behavior modification, and surgery.

Diet Therapy

Although dozens of weight reduction diets have been proposed for adults, most are not applicable to children. The goal of a weight reduction program in children must take into account normal growth and development and must preserve lean body mass. In children under one year of age, obesity is usually a result of overfeeding by the parents rather than demand by the infant. Dietary restriction may be indicated only after the parents are instructed to employ techniques other than the offering of food to meet the needs of the infant. Between the ages of one and five years, mild caloric restriction (approximately 10 per cent) in overweight children is adequate. In children older than five years a 10 to 25 per cent caloric restriction may be necessary with the goal of either stable weight while linear growth occurs, or weight loss of less than 0.5 pounds per week.[20] A technique suggested by Knittle is to limit caloric intake to 60 calories per kg of ideal body weight and to provide 20 per cent of calories as protein with the remaining 80 per cent evenly distributed between carbohydrate and fat.[50] Mineral and vitamin supplements are also provided. It is imperative that full cooperation be obtained from the patient's family (including siblings) and the school. Once dietary restriction is instituted, weight loss and linear growth must be carefully monitored.

Ideally, weight loss should be monitored in terms of body composition rather than total body weight.

In a study of 431 obese Italian children the investigators were able to induce a 30 per cent reduction of excess weight in approximately 60 per cent of the patients.[50] The diet consisted of 800 to 1200 calories depending on the patient's age. Two-thirds of the children with weight loss maintained their weight reduction for 18 to 24 months. In the 10 to 12 year old age group, 82 per cent demonstrated a sustained weight loss, whereas only 28 per cent of the six to nine year old group maintained their weight loss.

Drug Therapy

The ideal drug for the treatment of obesity would be one that suppresses the appetite controlling center of the hypothalamus. No drug has been shown to exert this effect in humans. Most physicians who treat childhood obesity would agree that drugs generally should be avoided.

Several classes of drugs have been employed, however, primarily in adults, as a means of appetite control. The sympathomimetic drugs are the principal agents used in the management of obesity, the most common representatives being the amphetamines. These agents have been shown to assist patients to adhere to a dietary regimen with subsequent weight loss; however, their effectiveness is transient.[26] They appear to be most effective when taken 1 to 1½ hours before a meal. It is difficult to demonstrate that amphetamines are true suppressants of appetite. Any effect they exert may be attributable to stimulation of the central nervous system which improves tolerance to hunger.[25] All amphetamine derivatives produce marked central nervous system stimulation except fenfluramine.[26] However, none of these sympathomimetic drugs has been recommended for use in children.

Various hormones or drugs affecting endocrine function have been used to treat obesity. Hormones such as thyroid, human chorionic gonadotropin, growth hormone, and progesterone have been used but are of questionable effectiveness. These medications may not be safe and therefore should not be used in childhood obesity.

Surgical Treatment

In the past decade surgical management of obesity has been employed extensively in adults; however, its use has been limited in children and adolescents. The two procedures currently used are jejunoileal bypass and gastric bypass. Massive intestinal bypass was the first operative procedure to be widely used in the treatment of morbid obesity.

Although extensive adult patient series have been reported, few published data are available on the use of operative intervention in the pediatric age range. Randolph et al.[45] in 1974 reported four cases of jejunoileal bypass, including one 11 year old boy with Prader-Willi syndrome who weighed 195 pounds and three girls, 15, 15, and 16 years old, who weighed 318, 404, and 437 pounds. Criteria for selection were similar to those proposed for adults: more than twice the ideal body weight for two years, failure of dietary therapy of at least one year, absence of a contribu-

tory metabolic disorder, assurance of patient and parent cooperation, and evidence of psychological stability as determined by a psychiatrist. The procedure used was an end-to-end jejunoileal bypass, anastomosing 14 inches of jejunum to four inches of terminal ileum. One year follow-up study showed an average weight loss of 33 per cent. There were no immediate postoperative complications. The authors reported that the 11 year old boy with Prader-Willi syndrome grew four inches in one year, suggesting that significant malabsorption may not affect growth and development. Subsequently, the same patient population with the addition of two more patients was reviewed in 1978.[19] The average weight loss at 30 months was 43 per cent. Liver enzymes were normal except for one patient who had an elevated serum gamma-glutamyl transpeptidase. The authors also reported that serum copper was low in four of eight patients and serum zinc was low in five of eight patients.

Gastric bypass (22 of 25) or gastroplasty (3 of 25) was employed by Soper et al. in 25 obese patients 20 years of age or younger (mean age 18 years).[53] There were 18 normal but obese adolescents and seven children with Prader-Willi syndrome. The mean weight for the entire group was 143 kg. Indications for surgery were: at least double the ideal weight for 5 years, absence of severe disease which would not be improved by weight loss, and absence of a primary endocrine cause of obesity.

The authors stated that "due to the natural history of the Prader-Willi syndrome, the twice ideal weight requirement for acceptance was not applied." Transfusions were required in seven patients in the intraoperative postoperative period. The median postoperative stay was nine days excluding those who required prolonged care for complications. The average weight loss for the patients with Prader-Willi syndrome was 16 per cent (range 3 to 34 per cent) in six of seven patients who lost weight. One patient with Prader-Willi syndrome gained weight (93 to 130 kg) over a four year period. Median weight loss for the obese but otherwise normal adolescents at six months, 15 months, 20 months and 36 months were 15, 30, 22, and 25 per cent, respectively. Postoperative complications were significant in this small series. Early complications included wound infection in three patients and respiratory difficulty in three patients, and thrombophlebitis, upper gastrointestinal bleeding, urinary tract infection, and protracted vomiting each occurred in one patient. The late complication of incisional hernia occurred in four patients. In addition, four patients required revisions of their initial operative procedure, one conversion of a gastroplasty to gastric bypass and three revisions of the gastric bypass.

According to Soper et al., the children who were still growing at the time of operation continued to grow in height at a normal rate postoperatively. It was also noted that some of the patients had a marked improvement in self-esteem.

Behavior Modification

Psychological, cultural, and familial determinants are only a few of the environmental factors which can influence eating patterns. During

the past two decades a variety of techniques based on learning theory and aimed at the modification of human behavior have been devised and evaluated. These techniques have been utilized in attempting to modify eating patterns. Preliminary data from these studies have been encouraging but not striking.[33, 47]

DISCUSSION

Obesity is one of the most common medical problems currently confronting the physician, as well as the general population. It is estimated that 10 million adolescents and young adults in the United States are obese and will remain so despite attempts at weight control.[28] This problem has received increased attention from those physicians involved in the primary care of children because: the onset of obesity in many adults occurred during infancy or childhood; there is evidence that the number of adipocytes can be influenced by overnutrition in childhood;[31] and obesity arising in childhood is notoriously resistant to treatment. No specific etiology for obesity in the human has been identified. It is likely that cellular, metabolic, socioeconomic, cultural, and psychological factors all interact to produce and maintain the obese state.

Because the etiology is unclear, treatment protocols are often confusing, ineffective, or risky. Management of obesity certainly must vary with age. Normal growth and development must be a primary concern in treating obesity in childhood. Weight reduction by definition must be catabolic and the impact of negative nitrogen balance, therefore, must be carefully observed. Dietary therapy appears to be the initial therapeutic approach and is likely to be most effective earlier in childhood. Drug therapy alone has little value; however, some authors have suggested that drug therapy in conjunction with dietary management did seem to improve results.[26]

Surgical intervention must be considered to be radical therapy for childhood obesity. Although continued growth in height was reported after jejunoileal bypass and gastric bypass, the series were very small.[33, 45] The metabolic derangements resulting from jejunoileal bypass certainly dictate that this procedure be used in extreme situations, if at all. Perhaps a more liberal view can be considered in the older adolescent. Gastric bypass produces fewer postoperative sequelae but the resulting weight loss is often not adequate. Also the psychological impact of postprandial vomiting may be significant in the pediatric age group.

Behavior modification appears to be a logical approach to management of obesity, regardless of the cause, but requires a significant commitment of time by the patient, family, and therapist. Initial weight loss is often followed by weight gain if intensive therapy is not continued.[27]

Prevention would appear to be the best long-term approach in dealing with obesity. However, this approach will require that physicians realize the significance of, and actively support, public education programs concerned with early onset of obesity.

REFERENCES

1. Abraham, S., Collins, G., and Nordsieck, M.: Relationship of childhood weight status to morbidity in adults. Public Health Rep., *86*:273, 1971.
2. Abraham, S., and Nordsieck, M.: Relationship of excess weight in children and adults. Public Health Rep., *75*:263, 1960.
3. Angel, J. L.: Constitution in female obesity. Am. J. Phys. Anthropol., *7*:433, 1949.
4. Asher, P.: Fat babies and fat children: The prognosis of obesity in the very young. Arch. Dis. Child., *41*:672, 1966.
5. Bar, R. S., Harrison, L. C., Roth, J., et al.: Insulin receptors in obesity. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
6. Bonnet, F., Duckerts, M., and Heuskin, A.: Subcutaneous adipose tissue growth in normal and obese children. *In* Laron, Z. (ed.): The Adipose Child. Pediatric and Adolescent Endocrinology, Vol. 1. Basel, S. Karger, 1976.
7. Bray, G. A.: The syndromes of childhood obesity. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
8. Brook, C. G. D.: Evidence for a sensitive period in adipose cell replication in man. Lancet, *2*:624, 1972.
9. Brook, C. G. D., and Lloyd, J. K.: Adipose cell size and glucose tolerance in obese children and effects of diet. Arch. Dis. Child., *48*:301, 1973.
10. Brook, C. G. D., Lloyd J. K., and Wolf, O. H.: Relation between the onset of obesity and size and number of adipose cells. Br. Med. J., *2*:25, 1972.
11. Brownell, K. D., and Stunkard, A. J.: Behavioral treatment of obesity in children. Am. J. Dis. Child., *132*:403, 1978.
12. Carnelutti, M., DelGuecico, N. J., and Chiumello, G.: Influence of growth hormone on the pathogenesis of obesity in children. J. Pediat., *77*:285, 1970.
13. Charney, E., Goodman, H. C., McBride, M., et al.: Childhood antecedents of adult obesity: Do chubby infants become obese adults? New Engl. J. Med., *295*:6, 1976.
14. Committee on Nutrition, American Academy of Pediatrics: Obesity in childhood. Pediatrics, *40*:455, 1967.
15. Dine, M., Gartside, P. S., Glueck, C. J., et al.: Where do the heaviest children come from? A prospective study of white children from birth to five years of age. Pediatrics, *63*:1, 1979.
16. Doyard, P. A., Chaussin, J. L., and Job, J. C.: Adipose tissue cellularity and hormonal data in obese children. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
17. Eid, E. E.: Follow up study of physical growth of children who had weight gain in the first six months of life. Br. Med. J., *2*:74, 1970.
18. Enzi, G., Inelmen, M., Cordioli, G., et al.: Fat cell size, weight and number in children in relation to anthropometric and metabolic parameters. *In* Laron, Z. (ed.): The Adipose Child. Pediatric and Adolescent Endocrinology, Vol. 1. Basel, S. Karger, 1976.
19. Faber, J., Randolph, J. G., Robbins, S., et al.: Zinc and copper status in young patients following jejunoileal bypass. J. Surg. Res., *24*:83, 1978.
20. Fomon, S. J.: Infant Nutrition. Philadelphia, W. B. Saunders Co., 1974.
21. Garn, S. M., Clark, D. C., and Guire, K. E.: Growth, body composition and development of obese and lean children. *In* Winick, M. (ed.): Childhood Obesity, Vol. 3. New York, John Wiley and Sons, 1975.
22. Galton, D. J.: The human adipose cell: A model for errors in metabolic regulation. New York, Appleton-Century-Crofts, 1971.
23. Ginsberg-Fellner, F., and Carmel, H.: The prevalence of obesity in nursery school children. Presented at the April 30, 1974 Plenary Session of the Ambulatory Pediatric Association.
24. Goldblatt, P. B., Moore, M. E., and Stunkard, A. J.: Social factors in obesity. J.A.M.A., *192*: 1039, 1965.
25. Grandguillaume, P., and Urech, E.: Obesity among school children. *In* Laron, Z. (ed.): The Adipose Child. Pediatric and Adolescent Endocrinology, Vol. 1. Basel, S. Karger, 1976.
26. Grollman, A.: Drug therapy of obesity in children. *In* Collipp, P. J. (ed.): Childhood Obesity. Acton, Mass., Publishing Sciences Group, Inc., 1975.
27. Hall, S. N.: Behavioral treatment of obesity: A two year follow up. Behav. Res. Ther., *2*:647, 1973.
28. Hammar, S. L.: Obesity and the pediatrician. Am. J. Dis. Child., *125*:787, 1973.
29. Hammer, S. L., Obesity: Early identification and treatment. *In* Collipp, P. J. (ed.): Childhood Obesity. Acton, Mass., Publishing Sciences Group, Inc., 1975.
30. Hetherington, A. W., and Ranson, S. W.: Hypothalamic lesions and adipocity in the rat. Ant. Rec., *78*:149, 1940.

31. Hirsch, J., and Knittle, J. L.: Cellularity of obese and nonobese human adipose tissue. Fed. Proc., *29*:1516, 1970.
32. Johnson, M. L., Burke, B. S., and Mayor, J.: The prevalence and incidence of obesity in a cross-section of elementary and secondary school children. Am. J. Clin. Nutr., 7:231, 1956.
33. Jordan, H. A., and Levitz, L. S.: Behavior modification in the treatment of obesity. Report of Second Wyeth Nutrition Symposium, Wyeth Laboratories, 1975.
34. Josefsberg, Z., Kauli, R., Keret, R., et al.: Growth hormone response to insulin tolerance and arginine stimulation in obese children and adolescents. *In* Laron, Z. (ed.): The Adipose Child. Pediatric and Adolescent Endocrinology, Vol. 1. Basel, S. Karger, 1976.
35. Knittle, J. L.: Obesity in childhood: A problem in adipose tissue cellular development. J. Pediat., *81*:1048, 1972.
36. Kornhaber, A., and Kornhaber, E.: Obesity in adolescents: Contributing psychopathological factors and their treatment. *In* Collipp, P. J. (ed.): Childhood Obesity. Acton, Mass., Publishing Sciences Group, Inc., 1975.
37. Lautala, P., Akerblom, H. K., and Kouvalainen, K.: The various types of insulin response to an oral glucose load in obese children. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
38. Lloyd, J. K., Wolf, O. H., and Whelen, W. S.: Childhood obesity: A long term study of height and weight. Br. Med. J., 2:145, 1961.
39. Mahler, R. J.: Islet cell hyperplasia and insulin insensitivity. *In* Levin, R., and Luft, R. (eds): Advances in Metabolic Disorders. New York, Academic Press, 1974.
40. Mellbin, T., and Vuille, J. C.: Physical development at seven years of age in relation to velocity of weight gain in infancy with special reference to incidence of overweight. Br. J. Prev. Soc. Med., 27:225, 1973.
41. Metropolitan Life Insurance Company: Frequency of overweight. Stat. Bull. Metropol. Life Ins. Co., *41*:4, 1960.
42. Pintor, C., Genazzani, A. R., Puggioni, R., et al.: The obese prepubertal girl: Plasma steroid patterns. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
43. Poskitt, E. M. E., and Cole, T. J.: Do fat babies stay fat? Br. Med. J., *1*:7, 1977.
44. Quabbe, H. J., Helge, H., and Jubicki, S.,: Nocturnal growth hormone secretion: Correlation with sleeping EEG in adults and pattern in children and adolescents with nonpituitary dwarfism, overgrowth and with obesity. Acta Endocrinol., 67:767, 1971.
45. Randolph, J. G., Weintraub, W. H., and Rigg, A.: Jejunoileal bypass for morbid obesity in adolescents. J. Pediat. Surg., *9*:341, 1974.
46. Ravelli, G., Stein, Z. A., and Susser, M. W.: Obesity in young men after famine exposure in utero and early infancy. New Engl. J. Med., 295:349, 1976.
47. Rivinus, T. M., Drummond, T., and Combrinck-Graham, L.: A group behavior treatment program for overweight children: Results of a pilot study. *In* Laron, Z. (ed.): The Adipose Child. Pediatric and Adolescent Endocrinology, Vol. 1. Basel, S. Karger, 1976.
48. Rogers, Q. R., and Leung, M. B.: The influence of amino acids on the neuroregulation of food intake. Fed. Proc., 32:1709, 1973.
49. Rony, H.: Obesity and Leanness. Philadelphia, Lea and Febiger, 1940.
50. Scavo, E., Giovannini, C., and Sellini, M.: Long and short term results of treatment for obesity in childhood and adolescence. *In* Cacciari, E., Laron, Z., and Raiti, S. (eds.): Obesity in Childhood. London, Academic Press, Inc., 1978.
51. Shukla, A., Forsyth, H. A., Anderson, C. M., et al.: Infantile over-nutrition in the first year of life, a field study in Dudley, Worcestershire. Br. Med. J., *4*:507, 1976.
52. Sidbury, J. B., Jr.: The metabolism of the adipocyte tissue: Possible role in obesity. Report of Second Wyeth Nutrition Symposium, 1975, p. 35.
53. Soper, R. T., Mason, E. E., Printen, K. J., et al.: Gastric bypass for morbid obesity in children and adolescents. J. Pediat. Surg., *10*:51, 1975.
54. Stunkard, A. J.: From explanation to action in psychosomatic medicine: The case of obesity. Psychosom. Med., 37:195, 1975.
55. Taitz, L. S.: Infantile overnutrition among artifically fed infants in the Sheffield region. Br. Med. J., *1*:315, 1971.
56. Tanner, J. N., and Whitehouse, R. H.: Revised standards for triceps and subscapular skinfolds in British children. Arch. Dis. Child., 50:142, 1975.
57. Udall, J. N., Harrison, G. G., Vaucher, Y., et al.: Interaction of maternal neonatal obesity. Pediatrics, 62:17, 1978.
58. Waxler, S. J., and Leef, M. F.: Obesity—Doctor's dilemma. Geriatrics, 27:98, 1969.

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Personality and Morbid Obesity

Implications for Dietary Management through Behavior Modification

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Psychological theories of the etiology of obesity include psychoanalytic formulations based on oral dependency needs because of a fixation at or a regression to the oral stage of development,[9] a proposed fundamental and profound disturbance in various aspects of early mother-infant interactions,[7] and learning theory conceptualizations of obesity as the result of a habit disturbance in which diverse environmental and emotional stimuli serve as highly conditioned cues for food intake.[14, 27] Investigations based on physiological theories have studied body weight regulation according to a set-point concept,[22] and there has been an increase in the past 10 years in research activity on the contribution of adipose cellularity at various stages of development to the determination of body weight.[43] Mayer and colleagues have studied the influence of constitutional and genetic factors, as well as physical activity levels, on the etiology of obesity.[38, 41] These research findings suggest that obesity is not a unitary syndrome and may be multidetermined, with several (although not mutually exclusive) types of obesity such as juvenile versus adult onset, moderate versus massive obesity, and psychodynamically determined eating disorders versus habit disorders. Different procedures may vary in their effectiveness in treating persons with these different types of obesity.

Practitioners have been cautioned to refrain from treating the symptom of obesity without dealing with the underlying causes of the disorder on the assumption that obesity is a depressive equivalent and that removing the symptom without treating the underlying cause will result in the manifestation of severe anxiety and depression.[6] However, the evidence on this issue suggests that if depression occurs during weight reduction, this emotional state is generally the result of the stress of diets that encourage rapid weight loss, or the stress of long-term inpatient fasting regimens.[53] The findings of investigations that carefully evaluated mood state during the weight reduction process have indicated that, in

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general, weight loss did not lead to an increase in depression[54] and actually led to decreases in both anxiety and depression for the weight reduction group as a whole.[17, 42] Mendelson suggested that obese persons may be classified on a continuum ranging from those who are emotionally stable to those in whom an eating disturbance is a central psychological issue in their lives.[39] Consistent with this formulation, numerous studies that have evaluated the psychological characteristics of obese persons have failed to find a consistent personality pattern or syndrome of underlying psychopathology, or consistent degrees of emotional maladjustment.[30]

PERSONALITY AND MORBID OBESITY

Morbid obesity can be viewed as a psychologically distinct type of weight disorder because of the generally long-term nature of the weight problem[28] and the marked difference presented by the individual's body build in a society that places a strong positive evaluation on thinness in females and a strong negative evaluation on the obese state. Obese children and adults have been rated as lazy, weak willed, and less acceptable for college than their moderate weight peers.[10, 32] However, personality evaluations of morbidly obese persons have failed to demonstrate a specific personality type or a consistent degree of psychopathology in this group. Minnesota Multiphasic Personality Inventory (MMPI) evaluation of 62 female patients prior to jejunoileal bypass surgery indicated generally normal psychiatric functioning with a tendency toward depression and somatization of emotional concerns.[28] A presurgical MMPI profile within the normal range was reported for a group of 70 morbidly obese persons.[55] The profile configuration suggested only mild personality disorders. Other investigators have reported varying degrees of depression, neurosis, personality disorder, several cases of schizophrenia, and quite normal psychological functioning in groups of patients evaluated prior to jejunoileal bypass surgery.[4, 11, 12, 21, 44] Although the majority of persons undergoing bypass surgery have been women, the psychological findings with the lesser number of male patients evaluated shows the same variety of adjustment and degrees of maladjustment.

The generally positive psychosocial changes that have been observed following intestinal bypass surgery suggest that the anxiety, depression, low self-esteem, and other psychological problems noted in many morbidly obese persons prior to weight loss may be the *result* of their obese state rather than the cause of it (see the article in this symposium by Halmi et al.[17a]). These various studies clearly demonstrate a systematic increase in self-esteem, body image, and personality evaluation, and greater independence and assertiveness as weight loss progresses. These findings confirm the fact that morbidly obese persons as a group are not impaired by serious psychiatric disturbance, and that the alleviation of the symptom of obesity markedly enhances psychological functioning.

The continuous eating behavior of the morbidly obese appears to be a fairly specific habit disturbance similar to other types of substance abuse problems such as alcoholism or drug addiction. The addictive nature of

this pattern was demonstrated by the findings of Leon et al. that the mean score of the morbidly obese patients on a scale that measures addiction proneness was just at the threshold indicative of an addiction problem.[28] The measure that was used is one that screens for addiction proneness and was standardized on groups of alcoholics and drug addicts.[16, 33] Further, those bypass patients who at the one year follow-up reported eating the same amount or more than they typically ate before surgery had relatively higher scores on this addiction measure than did the group that reported that they generally ate less at the follow-up than they had prior to surgery. Moderately obese persons did not score in the addictive range on this particular scale.[29] The strength of the habit disturbance in the morbidly obese in relation to food is also demonstrated by the fact that reanastomosis was followed by a return to the presurgical weight in all patients who required this procedure (see the article in this symposium by Buchwald[8]).

BEHAVIOR MODIFICATION FOR WEIGHT REDUCTION

Rationale

There has been a great surge of interest and enthusiasm over the past several years regarding the potential of behavior modification procedures for treating weight problems. Given the relative ineffectiveness of dietary, pharmacologic, and the more traditional psychotherapeutic techniques for treating obesity,[13, 25, 52] a treatment program based on established learning principles with initial reports of quite positive outcome held a great deal of promise. These procedures have substantial face validity in terms of the conception of obesity as based in part on a habit disturbance, and given the fact that habits have the potential of changing. On the other hand, the numbers of adipocytes, or the more subtle aspects of metabolism and the set point for body weight, are more permanent and unmodifiable aspects of an individual's constitution.[50]

The theory behind the various behavior modification treatment approaches is that both normal and abnormal behaviors follow the same laws of learning, that is, Pavlovian classical conditioning, operant or trial and error learning, and imitation learning. The behaviors or symptoms themselves are the target of treatment and modification, that is, overeating, eating high caloric foods, snacking between meals, and reduced levels of physical activity. The treatment is focused on these overt behaviors or habits rather than on hypothetical or presumed underlying emotional causes. This strategy implies that the symptoms or problem behaviors themselves may be the root of the disturbance, and that modifying the specific problem behaviors, in relation to food consumption, changes and therefore "cures" the problem.

Specific Procedures

Self-monitoring involves the process of instructing the patient to observe and record the problem behaviors in need of modification. For obese individuals, self-monitoring would consist of asking the patient to

keep a daily record of all instances in which food consumption occurred, including the type and amount of food eaten, the time of day food intake occurred, and the environmental and emotional circumstances at that time, such as eating in the living room or kitchen, in front of the television set, or eating when angry, bored, or frustrated. Self-monitoring is best used as a means of obtaining information about a person's eating patterns to aid in designating the behaviors in need of change. Self-monitoring is also effective as a means of feedback to the patient during the treatment program about his or her progress in changing habit patterns. Self-monitoring in itself has been demonstrated to have transient effectiveness in reducing food consumption,[2, 40] but the effect is short-lived without the addition of other behavioral procedures.

Stimulus control and environmental management are procedures that involve a change in surroundings in order to break the learned association between particular environmental cues and food intake, such as watching television and eating, or visiting with friends and eating. The individual is counseled to remove food from all places in the house except the kitchen, to lock up and make inaccessible excess foods, particularly high calorie snacks, and to eat each meal if possible in the same place and at the same time each day.[3, 48] The person is directed to place food portions directly on the plate before sitting down to eat rather than food being served "family style," to remove excess food from the table to avoid the temptation of taking a second helping, and to slow the pace of eating by chewing thoroughly and swallowing before taking another bite. Shopping from a grocery list to avoid impulsive purchasing is another aspect of programs of this type. Early reports of patients treated by these procedures were extremely positive and indicated a weight loss of 26 to 47 pounds over a one year period.[47]

Positive reinforcement refers to the presentation of a reward following the occurrence of a specified behavior. A reward or reinforcer is operationally defined as anything that increases the frequency of the particular response the reward is applied to. In behavioral weight reduction programs, the reward may be material, such as a designated amount of money that is either spent or saved for a future (non-food) treat. A reward is earned according to a specified schedule of losing weight or changing particular eating patterns; this type of reward system has been used effectively in a number of investigations.[34, 36] Social approval by one's spouse or family for particular behavior changes can also be a very potent source of positive reinforcement, and a number of recent studies have included the spouse in the treatment program. Cooperative spouses have been trained to facilitate their partner's weight reduction through the systematic use of encouragement and social approval for appropriate eating habit changes. The treatment outcome data, however, indicate mixed results in terms of the long-term maintenance of the weight loss with spouse support systems.[5, 19, 24]

Contingency contracting is an agreement between the therapist and the patient, specifying the problem behaviors to be changed and the consequences that will be applied if the behavioral change does or does not occur.[18, 37] The contract can be drawn up with particular reinforcers

agreed upon, contingent on the occurrence of positive behavior changes (such as refraining from snacking or losing a specific number of pounds per week). A dual reward-penalty contract also has been used. Mann reported on an individualized contingency contract in which the person designated valued items that were left with the therapist and either earned back or permanently lost depending on the progress of weight reduction.[37] However, the use of strongly negative contingencies may result in the individual closely adhering to the weight reduction program while the contingency is in effect, but then regaining the lost weight after the contingency condition has been removed.

Aversive conditioning is a procedure employed to develop a negative or unpleasant association to a previously neutral or positively conditioned stimulus such as carrying out a problem eating behavior or even thinking about consuming particular foods. Aversive techniques that have been used for weight reduction include subjecting the person to a foul smelling odor[15] or a brief electric shock[46] immediately preceding the presentation of a craved-for food. A conditioned response is then established between the aversive stimulus and the food. Instructing the patient to look at himself or herself unclothed in front of a full-length mirror and then visualize this image each time the person is tempted to eat inappropriately is an example of aversive imagery. Treatment outcome studies indicate that the odor and shock procedures have not been effective in maintaining weight loss, primarily because persons generally do not overeat just one type of food nor can they completely stop eating. Persons who are overweight must learn in some way to monitor food intake, plan what they are going to eat, and then develop new and more adaptive eating patterns if they are to maintain weight loss.[25]

Evaluation of Efficacy of Treatment

There are a variety of techniques ranging from jaw-wiring and diets to total starvation that are effective in short-term weight loss as long as the patient adheres to the particular treatment regimen. However, the long-term maintenance of weight loss is a crucial consideration and seems to be the only adequate criterion to use in assessing treatment efficacy.

Reviews of the outcome studies of behavior modification programs that have employed positive reinforcement and self-management strategies aimed at changing eating patterns indicate that these particular programs are more effective than other currently existing procedures for weight reduction except surgical intervention.[20, 25] However, these behavior modification programs produce on the average only modest weight losses of between seven and 16 pounds by the end of treatment, and frequently there is an erosion of this weight loss over a one year follow-up period. The addition of booster sessions during the maintenance period shows inconsistent results in the maintenance of weight loss.[1, 23] However, the addition of a daily exercise component appears to increase the effectiveness of behavioral programs.[45]

Self-Control Strategies

The relatively modest effectiveness to date of behavioral programs

has stimulated researchers to add self-control components to the behavior modification "treatment package." Self-control strategies focus on teaching persons to refrain from food consumption through employing specific behavioral and cognitive procedures for controlling one's behavior when there is a temptation or urge to eat.[35] Individuals learn to be more aware of and to monitor the thoughts or self-statements that typically lead to food consumption and to substitute more adaptive imagery or thought sequences in order to refrain from eating. For example, if it is determined that a high caloric snacking chain begins by the self-statement: "What's the difference if I eat one donut? I'll just take this one and then I'll stop," the person would be taught to make the following nonverbal self-statement: "No. Don't eat this. Eating one donut leads to eating still more food." The person might also be counseled to walk out of the room in which there are cues tempting one to eat or to get involved in some other activity that serves as a distraction from the urge to eat.[31]

Self-control counseling also includes an exploration of the decision-making process and the commitment to change one's problem behavior patterns.[26] These changes can only occur if persons are willing to make the necessary behavioral alterations; the issue of motivation therefore has to be included in any type of self-help program.

Long-term changes in eating patterns may be best accomplished if accompanied by changes in other aspects in one's life, such as increasing levels of physical activity, spending less time in front of the television set, and substituting low caloric foods for the high caloric meals and snacks the person or family might typically eat. In order to maintain healthy weight levels effectively, it may be necessary for the entire family to adopt these changes in life-style. It is important to refrain from viewing these modifications as a temporary feature, such as a diet that one expects to adhere to for only a limited period of time.

Behavior Modification Management of Morbidly Obese Persons

Morbidly obese persons do not seem to be good candidates for behavior modification weight reduction programs because of the relatively small amount of weight generally lost in programs of this nature. However, as in any treatment regimen, a few individuals may lose a substantial amount of weight. Some massively obese persons have reached their goal weight through self-help programs such as TOPS,[51] and as members of commercial weight reduction clubs.[49] Therefore, the patient should be encouraged to learn to implement the various behavioral techniques and try to adhere to the particular program.

The large quantity of food that morbidly obese individuals must eat to maintain that degree of obesity points to a substance abuse component of this particular disorder. Some alcoholics and drug addicts are able to overcome habit disturbances through orienting their lives around the alleviation of these particular problems, that is, by becoming extremely active in groups such as Alcoholics Anonymous and other types of counseling groups. Similarly, many individuals who have been morbidly obese and have been successful in losing and maintaining a significant weight loss have also become active as lecturers and group leaders in various

weight reduction clubs. These activities continually remind the person of the commitment to change his or her eating patterns and life-style, and provide extremely strong social support or reinforcement for maintaining the weight loss.

However, the majority of morbidly obese persons have tried many types of diets and treatment programs and have been unable to adhere to these regimens for an indefinite period of time. In a sense, morbidly obese persons are the exemplification of the failure of nonsurgical methods for treating severe obesity problems. Therefore, after it has been ascertained that the patient has tried other methods of weight reduction and has failed in these attempts, bypass surgery would seem to be a viable alternative. The enhanced psychological and social functioning of the majority of persons who have undergone this procedure is impressive.[28] However, it is important to have counseling services available for those individuals who might experience personal, marital, or other family conflicts as a result of their dramatic weight reduction and the concomitant changes in self-image after surgery.

SUMMARY

Psychological investigations have failed to reveal a distinct personality type or psychodynamic conflict pattern in moderately and massively obese persons. Many of the psychological problems noted in the obese such as anxiety, depression, and poor self-esteem seem to be the result of, rather than the cause of, the obese state. Morbidly obese persons share an addictive behavior pattern that is also seen in persons with other types of addictions. The extent of their obesity points to the strong substance abuse component of the eating disorder. Behavior modification programs aimed at changing problematic eating patterns and teaching self-management skills in relation to food consumption have been moderately successful and have been shown to result in a mean post-treatment weight loss of seven to 16 pounds. However, the majority of morbidly obese persons will not lose enough weight to make this an effective treatment program for them.

REFERENCES

1. Ashby, W. A., and Wilson, G. T.: Behavior therapy for obesity: Booster sessions and long-term maintenance of weight loss. Behav. Res. Ther., *15*:451, 1977.
2. Bellack, A. S., Rozensky, R., and Schwartz, J.: A comparison of two forms of self-monitoring in a behavioral weight reduction program. Behav. Ther., 5:523, 1974.
3. Beneke, W. M., Paulsen, B., McReynolds, W. T., et al.: Long-term results of two behavior modification weight loss programs using nutritionists as therapists. Behav. Ther., *9*:501, 1978.
4. Brewer, C., White, H., and Baddeley, M.: Beneficial effects of jejeunoileostomy on compulsive eating and associated psychiatric symptoms. Br. Med. J., *4*:314, 1974.
5. Brownell, K. D., Heckerman, C. L., Westlake, R. J., et al.: The effect of couples training and partner cooperativeness in the behavioral treatment of obesity. Behav. Res. Ther., *16*:323, 1978.
6. Bruch, H.: Psychological aspects of overeating and obesity. Psychosomatics, 5:269, 1964.
7. Bruch, H.: Family transactions in eating disorders. Comp. Psychiatry, *12*:238, 1971.

8. Buchwald, H.: Surgical approaches for failed jejunoileal bypass and failed gastric bypass. SURG. CLIN. NORTH AM., *59*:000, 1979.
9. Bychowski, G.: On neurotic obesity. Psychoanal. Rev., *37*:301, 1950.
10. Canning, H., and Mayer, J.: Obesity: Its possible effect on college acceptance. New Engl. J. Med., *275*:1172, 1966.
11. Castelnuovo-Tedesco, P., and Schiebel, D.: Studies of superobesity. II. Psychiatric appraisal of jejuno-ileal bypass surgery. Am. J. Psychiatry, *133*:26, 1976.
12. Espmark, S.: Psychological adjustment before and after bypass surgery for extreme obesity—A preliminary report. *In* Howard, A. (ed.): Recent Advances in Obesity Research I. Proceedings of the First International Congress on Obesity. London, Newman Publishing, 1975.
13. Feinstein, A. R.: The treatment of obesity: An analysis of methods, results, and factors which influence success. J. Chron. Dis., *11*:349, 1960.
14. Ferster, C. B., Nurnberger, J. I., and Levitt, E. B.: The control of eating. J. Mathematics, *1*:87, 1962.
15. Foreyt, J. P., and Kennedy, W. A.: Treatment of overweight by aversion therapy. Behav. Res. Ther., *9*:29, 1971.
16. Fowler, R.: A method for evaluation of the abuse prone patient. Chicago, American Academy of Family Physicians, 1975.
17. Graff, H.: Overweight and emotions in the obesity clinic. Psychosomatics, *6*:89, 1965.
17a. Halmi, K. A., Stunkard, A. J., and Mason, E. E.: Emotional responses to weight reduction by three methods: Gastric bypass, jejunoileal bypass, diet. SURG. CLIN. NORTH AM., *59*: 1979.
18. Harris, M. B., and Bruner, C. G.: A comparison of a self-control and a contract procedure for weight control. Behav. Res. Ther., *9*:347, 1971.
19. Israel, A. C., and Saccone, A. J.: Follow-up effects of choice of mediator and target or reinforcement on weight loss. Behav. Ther., *10*:260, 1979.
20. Jeffrey, R. W., Wing, R. R., and Stunkard, A. J.: Behavioral treatment of obesity: The state of the art 1976. Behav. Ther., *9*:189, 1978.
21. Kalucy, R. S., and Crisp, A. H.: Some psychological and social implications of massive obesity. J. Psychosom. Res., *18*:465, 1974.
22. Keesey, R. E.: Set-points and body weight regulation. Psych. Clin. North Am., *1*:523, 1978.
23. Kingsley, R. G., and Wilson, G. T.: Behavior therapy for obesity: A comparative investigation of long-term efficacy. J. Consult. Clin. Psychol., *45*:288, 1977.
24. Kolotkin, R.: Assertion training, spouse involvement, and individual differences in a cognitive-behavioral treatment of obesity. Unpublished doctoral dissertation, University of Minnesota, 1978.
25. Leon, G. R.: Current directions in the treatment of obesity. Psychol. Bull., *83*:557, 1976.
26. Leon, G. R.: Cognitive-behavior therapy for eating disturbances. *In* Kendall, P., and Hollon, S. (eds.): Cognitive-Behavioral Interventions: Theory, Research, and Procedures. New York, Academic Press, 1979, in press.
27. Leon, G.R., and Chamberlain, K.: Emotional arousal, eating patterns, and body image as differential factors associated with varying success in maintaining a weight loss. J. Consult. Clin. Psychol., *40*:474, 1973.
28. Leon, G.R., Eckert, E. D., Teed, D., et al.: Changes in body image and other psychological factors after intestinal bypass surgery for massive obesity. J. Behav. Med., 2:39, 1979.
29. Leon, G. R., Kolotkin, R., and Korgeski, G.: MacAndrew addiction scale and other MMPI characteristics associated with obesity, anorexia, and smoking behavior. Addictive Behav., 1979, in press.
30. Leon, G. R., and Roth, L.: Obesity: Psychological causes, correlations and speculations. Psychol. Bull., *84*:117, 1977.
31. Leon, G. R., Roth, L., and Hewitt, M. I.: Eating patterns, satiety, and self-control behavior of obese persons during weight reduction. Obes. Bariat. Med., *6*:172, 1977.
32. Lerner, R. M., and Gellert, E.: Body build identification, preference, and aversion in children. Develop. Psychol., *1*:456, 1969.
33. MacAndrew, C.: The differentiation of male alcoholic outpatients from nonalcoholic psychiatric patients by means of the MMPI. Quart. J. Stud. Alcoh., *26*:238, 1965.
34. Mahoney, M. J.: Self-reward and self-monitoring techniques for weight control. Behav. Ther., 5:48, 1974.
35. Mahoney, M. J., and Mahoney, K.: Permanent Weight Control. New York, W. W. Norton, 1976.
36. Mahoney, M. J., Moura, N. G., and Wade, T. C. Relative efficacy of self-reward, self-punishment, and self-monitoring techniques for weight loss. J. Consult. Clin. Psychol., *40*:404, 1973.
37. Mann, R. A. The behavior-therapeutic use of contingency contracting to control an adult behavior problem: Weight control. J. Appl. Behav. Anal., 5:99, 1972.

38. Mayer, J.: Inactivity as a major factor in adolescent obesity. Ann. N.Y. Acad. Sci., *131*:502, 1965.
39. Mendelson, M.: Psychological aspects of obesity. Int. J. Psychiatry, 2:599, 1966.
40. Romancyzk, R. G.: Self-monitoring in the treatment of obesity: Parameters of reactivity. Behav. Ther., 5:531, 1974.
41. Seltzer, C. C., and Mayer, J.: Body build (somatotype) distinctiveness in obese women. J. Am. Diet. Assoc., 55:454, 1969.
42. Silverstone, J. T., and Lascelles, B. D.: Dieting and depression. Br. J. Psychiatry, *112*:513, 1966.
43. Sjöström, L.: The contribution of fat cells to the determination of body weight. Psych. Clin. North Am., *1*:493, 1978.
44. Solow, C., Silberfarb, P. M., and Swift, K.: Psychosocial effects of intestinal bypass surgery for severe obesity. New Engl. J. Med., *290*:300, 1974.
45. Stalonas, P. M., Jr., Johnson, W. G., and Christ, M.: Behavior modification for obesity: The evaluation of exercise, contingency management, and program adherence. J. Consult. Clin. Psychol., *46*:463, 1978.
46. Stollak, G. E.: Weight loss obtained under different experimental procedures. Psychother. Theor. Res. Prac., *4*:61, 1967.
47. Stuart, R. B.: Behavioral control of overeating. Behav. Res. Ther., 5:357, 1967.
48. Stuart, R. B.: A three-dimensional program for the treatment of obesity. Behav. Res. Ther., *9*:177, 1971.
49. Stuart, R. B., and Mitchell, C.: Self-help weight control groups: A professional and a consumer perspective. *1*:697, 1978.
50. Stunkard, A. J. (ed.): Symposium on Obesity: Basic Mechanisms and Treatment. Psych. Clinics of North Am. *1*:459–732, 1978.
51. Stunkard, W., Levine, H., and Fox, S.: The management of obesity. Arch. Intern. Med., *125*:1067, 1970.
52. Stunkard, A. J., and McLaren-Hume, M.: The results of treatment for obesity. Arch. Intern. Med., *103*:79, 1959.
53. Stunkard, A. J., and Rush, J.: Dieting and depression reexamined. Ann. Intern. Med., *81*:526, 1974.
54. Taylor, C. B., Ferguson, J. M., and Reading, J. C.: Gradual weight loss and depression. Behav. Ther., *9*:622, 1978.
55. Webb, W. W., Phares, R., Abram, H. S., et al.: Jejunoileal bypass procedures in morbid obesity: Preoperative psychological findings. J. Clin. Psychol., 32:82, 1976.

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Energy Regulation in Morbid Obesity by Multidisciplinary Therapy

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The increased incidence and severity of obesity in this country have been a subject of both medical and governmental attention. It is difficult to determine the exact prevalence of obesity because of varying definitions. The McGovern Committee has considered 30 to 40 million Americans to be overweight.[31] The National Center for Health Statistics of the United States Public Health Service reports that almost three million men and four and one half million women are severely obese that is, 30 to 50 per cent above "relative desirable" weight.[46] Morbid obesity describes a particular subgroup of obese patients who weigh at least 300 pounds, or are 100 pounds overweight, or weigh more than 200 per cent of their desirable weight based on standard weight/height charts.[32] It is this group of patients for whom obesity is a major risk factor in the development of various chronic illnesses (Table 1) and for whom there is a dramatic increase in mortality rates based on age and sex-matched life expectancy tables.

There is no clear understanding of the underlying etiology of obesity. There are competing theories regarding the relative role of environmental factors and maladaptive behavior, metabolic factors, and genetic influences. Although obesity should be considered to be a multifactorial disease, neither metabolic nor genetic influences seem to be primarily at fault in the majority of patients.

Recognizing the importance of environmental determinants, a great deal of justified attention has been focused on the change in energy expenditure and patterns of food consumption over the past century, both

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Table 1. *Conditions Associated with Morbid Obesity*[24]

Diabetes mellitus	Degenerative arthritis
Hypertension	Gallbladder disease
Coronary heart disease	Infertility
Congestive heart failure	Hyperlipoproteinemia
Restrictive lung disease	Psychosocial incapacity
Pickwickian syndrome	

in terms of caloric consumption and food group distribution. Although total caloric consumption has declined, a greater decline in activity levels has occurred along with a proportional increase in intakes of fat and refined carbohydrates. In addition to such epidemiologic considerations, recent research has also explored the nature of adipocyte expansion.[21] This expansion may occur by an increase in the number of cells or an increase in the size of cells. Characterization of the timing of hypertrophic or hyperplastic fat accumulation may improve the understanding of treatment difficulties.

Most severely obese patients have experimented with a variety of medical techniques of weight loss without success. Short-term weight reduction of greater than 18 kg is reported in fewer than 5 per cent of outpatients who diet under some supervision.[44] The enormous success and profitability of the "diet industry," including best sellers, commercial diet salons, appetite depressant medications,[11, 12] and a variety of other methods confirm this sad state of affairs.[10, 18, 30] The difficulty of dietary treatment is further emphasized by the high rate of recidivism documented in long-term follow-up studies.[19]

Initial reports of an integrated approach that includes behavior modification and modified fasting in moderately obese (approximately 130 to 200 per cent desirable body weight) patients have been promising.[8] Bistrian found that one third of patients maintained a weight loss greater than 18 kg four years following treatment.[2] Additional follow-up studies will be needed to confirm these findings but the current results support the use of comprehensive multidisciplinary approaches to obesity.[7]

For morbidly obese patients, no conservative treatment program has resulted in successful long-term weight reduction. The recent National Institutes of Health Consensus Development Conference on Surgical Treatment in Morbid Obesity characterized these patients as those with serious physical and psychosocial problems who have failed to improve on adequate trials of nonsurgical treatment or who have repeatedly relapsed after initial periods of weight loss.[46] Surgery may then be viewed as a final attempt at weight control in which the risks inherent to the procedure are accepted as an alternative to a life of incapacity, dysfunction, and accelerated mortality. Criteria for surgical treatment are outlined in Table 2.[24] Unlike other surgical procedures to correct underlying organic disorders, surgical treatment of obesity does not offer a cure. It is one part of a labor-intense, high risk, and expensive approach to the rehabilitation of the morbidly obese patient. Operative intervention can offer an essential and remarkably effective element of control, within a total program aimed

Table 2. *Criteria for Surgical Treatment of Morbid Obesity*[24]

Weight more than 200 per cent of standard for height, sex, and age.
Repeated failure of dietary control or inability to adhere to dietary methods.
Stable adult life pattern.
Between 18 and 50 years of age
Absence of serious heart disease, inflammatory bowel disease, or significant hepatic or renal dysfunction.

at reducing organic complications and correcting psychosocial disorders[37] which mark the lives of these patients.

Knowledge of energy expenditure is most important in treatment of morbid obesity by surgical intervention, the management alternative that yields the highest incidence of sustained weight loss. Surgical treatment programs offer the greatest improvement in quality of life of the various therapeutic options available. Surgical procedures, however, must be seen not as unimodal therapy, but within the context of a comprehensive treatment program involving changes in energy intake and expenditure. Surgical treatment without attention to the other multifaceted problems of morbidly obese patients, including continued caloric control of diet, family interaction, and behavioral-psychological profiles, increases the risk of poor long-term results. Surgery is only a functional adjunct to comprehensive obesity therapy, which must include nutritional education, diet counseling, exercise planning, and behavior therapy.[8, 18] A successful program can usually be measured by a 10 to 15 pound monthly weight loss for nine to 15 months. Lesser results may reflect unwarranted attention to surgery alone.

COMPREHENSIVE WEIGHT CONTROL PROGRAM IN PREPARATION FOR GASTRIC BYPASS SURGERY

A comprehensive approach to weight loss and weight maintenance involves three priorities: cue control and food avoidance behavior change; establishment of increased activity patterns; and a technique specifically used to produce weight loss. It is important that this order of priorities be understood lest a comprehensive program be misinterpreted with undue attention placed on the surgical approach for weight loss.

The details of a protein-sparing modified fast suitable for preoperative preparation have recently been reviewed.[2] Protein sparing requires the provision of approximately 1.5 gm of protein per kg of ideal body weight per day, together with appropriate vitamins and minerals, particularly potassium, phosphate, and magnesium. Use of severe calorie-restricted diets (less than 800 kcal per day) preoperatively results in certain physiologic and metabolic changes. These primarily involve reduction in blood volume during the first weeks of fasting with the potential for postural hypotension which can be hazardous if not managed properly.[2] Such regimens can be used preoperatively for several favorable metabolic changes associated with semistarvation[6] and the progressive shift of

metabolism to a fat-based fuel economy, wherein the catabolism of ketone bodies meets 80 per cent of the energy needs of the brain. This state has been associated with improved respiratory function in patients with alveolar hypoventilation.[17] The natriuresis associated with ketonuria[42] limits the expansion of total body water which may also aid cardiorespiratory function. The ability to develop and maintain ketonuria in the postoperative period may serve as an early metabolic monitor of the effective adaptation to starvation.[33] In some individuals at high surgical risk, a more prolonged dietary period before surgery may be desirable.

Program Overview

At the initial interview of the patient, the staff is introduced and each member's special area of expertise is explained. Attention is given to the reasonable expectations from the comprehensive treatment of obesity, whether the treatment includes surgery or not. The steps involved in the program, its significance, and its rationale are explained, and the unique patient-physician "partnership" based on shared responsibilities is emphasized.

Intake evaluation includes not only physical examination and routine biochemical and metabolic tests, but also psychological testing,[7] exercise fitness assessment, and nutritional history. Three-day food activity diaries are completed and the patient is begun on a standard American Dietetic Association balanced-deficit diet, monitored for compliance, daily planning capacity, and record keeping. The patient is also monitored during the intake period for blood pressure, weight, mood changes, subjective feelings, and understanding of the goals and objectives of the program and the risks and benefits of surgery.

The patient is maintained on a balanced-deficit diet of 1000 to 1200 kcal per day for three to four weeks to demonstrate the potential for weight loss. He or she takes the responsibility of self-monitoring techniques, allowing the staff to evaluate the reliability and compliance with all aspects of the program (diet, exercise, behavior modification, and so forth). During this period, low but progressively more demanding exercise regimens are introduced. A family meeting is arranged to explain the program, emphasize the importance of *positive* family interactions, explain the role of surgery, and discuss concerns regarding obesity, responsibilities, and expectations. In approximately four to six weeks, all the intake data have been collected and the patient has had ample time to consider the program. If there is still agreement among patient, family, surgeon, physician, psychologist, and patient-advocate that surgery is an appropriate adjunct to the patient's comprehensive program, the preoperative preparation of the patient is begun so that hospitalization will be as short as possible.

Except for the two to three weeks to recover from surgery, the patient is maintained in the medical program. This requires weekly attendance at seminars, tutorial sessions, and group sessions designed to improve the knowledge and capacity to use behavior modification techniques, exercise physiology, and nutritional education. The physician and psychologist perform all special medical and therapeutic evaluations and

treatments. Every effort is directed at reinforcing the available resources for weight maintenance once weight loss has been achieved.

In patients in whom a more prolonged regimen of weight loss is necessary to reduce operative risk, inpatient or outpatient use of a semistarvation ketogenic regimen may be employed for a variable period. Inpatient programs of up to several weeks' duration may be used for individuals with problems such as severe alveolar hypoventilation, or for patients taking drugs such as insulin[5] or multiple or large doses of antihypertensives[2] which could be reduced or eliminated prior to surgery. Outpatient programs using semistarvation regimens are reserved for those without serious medical complications, other than obesity, whose acceptance for bypass surgery is in part tied to successful weight reduction preoperatively.

MANAGEMENT DURING HOSPITALIZATION

Once the patient has progressed through the above initial phases of comprehensive management of obesity, it may be agreed that a surgical procedure is a realistic component of the total treatment plan. Careful discussions of the potential risks, benefits, and uncertainties of gastric bypass surgery are continued. The details of the procedure are outlined for the patient. Other significant family members are involved in the discussions. Occasionally, once informed of the complexity and risks related to bypass procedures, a patient will decide to defer surgery. In some instances, this has provided a cognitive avoidance stimulus to enhance motivation for conservative nonsurgical treatment plans.

As an important component of truly informed consent, a physician not involved with the surgery (such as an internist, endocrinologist, psychiatrist) also reviews with the patient the surgical approach and tries to clarify areas of uncertainty and elaborate the alternatives to surgical intervention. Frequently, an independent patient-advocate, someone other than those dealing directly with the obesity problem, may advise the patient. In addition, opportunities are provided for the patient considering surgical treatment to meet with patients who have already undergone bypass procedures, both with and without long-term weight reduction or postoperative complications.

Once the decision for surgical intervention is made, the necessary admission and preoperative studies are arranged in order to minimize the length of the hospital stay (Table 3). Laboratory testing upon admission includes routine hematologic and coagulation studies and automated chemistry profiles. A chest x-ray film and urinalysis are obtained along with an electrocardiogram. Limited pulmonary function testing is done in conjunction with sampling of room-air arterial blood gases. A double-dose oral cholecystogram and upper gastrointestinal series are performed the morning after admission. The purpose of the cholecystogram is to exclude gallbladder disease since there is an increased incidence of cholelithiasis in obese patients,[11] especially in those who have utilized certain lithogenic diet techniques.[22] The upper gastrointestinal series demonstrates unsus-

Table 3. *Preoperative Preparations*

1. The following studies are completed or data collected:
   - Office
     - HELP Medical History and Physical Status Form
     - Obesity Questionnaire: Short and Long (Lindner) Forms
     - Minnesota Multiphasic Personality Inventory/Profile of Mood States/Stress Index
     - Astrand Exercise Bicycle Test
   - Hospital
     - Inpatient or admission laboratory tests, including:
       - Chem 18; CBC with differential; urinalysis; platelet count; T_4; triglycerides; PT/PTT; and HDL cholesterol
     - Chest x-ray, upper GI series, double-dose oral cholecystogram
     - Electrocardiogram
     - Pulmonary function tests: Short form with room air arterial blood gases
     - Phleborheography
2. Mini-dose heparin: 5000 units every 12 hours
3. Bowel preparation: Fleet's enema evening before surgery
4. Intravenous catheter, preferably central (subclavian or internal jugular) with normal saline. Start intravenous evening prior to surgery if early case, or early morning if afternoon case.
5. Cephalosporin, 1 gm intravenously, with preoperative medications

pected hiatal hernia, peptic ulcer disease, or anatomic variations within the stomach or first portion of the small intestine which may affect the bypass operation. The patient receives a cathartic following the upper gastrointestinal series to avoid barium stasis in the colon in the perioperative period. In many patients it is possible to obtain the radiologic examinations on an outpatient basis. If the oral cholecystogram shows inadequate visualization of the gallbladder, an abdominal ultrasound examination is arranged shortly after admission to help exclude cholelithiasis. Although the gallbladder is routinely palpated intraoperatively, the physical characteristics of the patient and the usually full, somewhat distended status of the gallbladder limit the reliability of intraoperative examination.

Pulmonary function testing consists of limited forced ventilation tests, including forced expiratory volume, forced vital capacity, maximum voluntary ventilation, peak flow rate, and maximum mid-expiratory flow rate. The more complex resting ventilation studies are not routinely done. An arterial blood gas sample is also obtained. These studies together provide a baseline to characterize the respiratory function of the patient in terms of both ventilation and oxygenation. With these examinations, it is possible to estimate the abnormality caused by obesity, which is usually restrictive in nature, and to determine the normal level of oxygen and carbon dioxide for the individual patient. These figures provide a relative set point for ventilator management if there is difficulty in weaning the patient from the respirator in the postoperative period. Patients with restrictive disease, in particular, are also taught to use incentive spirometry prior to surgery.

After the admission laboratory tests (including a "coagulogram")* are

*Prothrombin time, partial thromboplastin time, antithrombin III level, and platelet count.

obtained, mini-dose heparin prophylaxis is initiated because of the increased risk of thrombotic phenomenon in obese patients.[11] Patients with normal clotting systems often become hypercoagulable during relative or absolute restriction of activity, as the normal balance between clot formation and fibrinolysis becomes temporarily unbalanced by reduced activity.[45] This is another reason for minimizing the duration of the preoperative hospital stay and insisting on early postoperative ambulation. The mini-dose heparin may not be utilized if there is any relative contraindication, such as recent use of aspirin for arthritis of weight-bearing joints commonly seen in the morbidly obese. A pilot study is under way to evaluate the usefulness of phleborheography[16] in predicting the need for heparin in obese patients.

ENERGY REGULATION IN THE OPERATIVE PERIOD

The preoperative diet depends on the anticipated length of time before operation. If the patient has been adapted to a protein-sparing modified fast as an outpatient, it is simply continued after admission. If the patient is to undergo operation within a day or two of admission and has been on a regular diet, a reduced carbohydrate diet is used. If the patient requires several days of hospitalization, a protein-sparing modified fast (PSMF), high protein (1.5 gm per kg per day) diet is usually begun because of its beneficial effects. These effects, described earlier in this review, include reduction of insulin requirements, reduction of blood pressure secondary to the natriuresis that occurs, and early mobilization of glycogen and fat from the liver. It may be difficult to comply exactly with the PSMF as originally described because of the preparation diets required for the above radiologic examinations, but a limited carbohydrate diet provides nearly as much benefit.

The patient is introduced to the individuals of the hospital-based team: the surgeon and his associates, the resident and nursing staff, the dietitian involved in both preoperative and postoperative teaching, the nursing members of the Nutrition Support Service, and the respiratory care technicians involved in preoperative instruction and postoperative pulmonary toilet. A hospital pamphlet which discusses the procedures involved in surgery is also provided. A well-informed patient can be properly relaxed and reassured, resulting in more effective use of analgesic drugs and cooperation with orders for ambulation and respiratory care.

On the evening before operation, an intravenous infusion is started in order to ensure adequate hydration at the beginning of the operation. Depending on the anxiety and cooperation of the patient, a central intravenous line may be inserted at this time. A cleansing enema the evening before surgery is ordered to completely empty the colon. In addition to the usual preoperative medications provided by the anesthesia department, antibiotic prophylaxis is begun with a single dose of a cephalosporin on call to the operating room. The antibiotic is continued intraoperatively and for a brief time postoperatively.

TECHNICAL CONSIDERATIONS FOR GASTRIC BYPASS

The actual steps involved in gastric bypass operation have evolved gradually over the past decade. Since the operation was initially proposed by Mason in the mid-1960s,[28] each of the changes introduced derive from the increasing experience of those groups which have cared for a large number of patients and are committed to achieving optimal results within the framework of ongoing evaluation. Our early review of such technical considerations is published elsewhere.[25] Additional modifications have been introduced, based on our own findings and recommendations of others in the field.

After induction of general anesthesia, additional monitoring devices are applied. A urinary catheter is inserted to follow urinary output during operation. If not already done, the central venous catheter is placed, usually by an internal jugular approach. If preoperative testing indicates significant respiratory impairment, a radial artery cannula is inserted, either percutaneously or by cutdown. After the usual antiseptic skin preparation and draping, a midline incision is made, although bilateral subcostal incisions have been used. Once the skin is incised, the subcutaneous fat is separated bluntly as recommended by Mason,[26] the peritoneum is entered, and the abdomen is completely explored. Following manual exploration, retractors are arranged. A recently devised self-retaining circular retraction system has markedly improved access.[14] This retractor system eliminates the numerous assistants previously required to give adequate exposure and allows the operation to be performed without difficulty by two operators.

With a large nasogastric tube or Ewald tube in place, the dissection of the cephalad portion of the greater curvature of the stomach is begun. This dissection starts at the level of the short gastric arteries, which are subsequently isolated, ligated, and divided in continuity moving upward along the greater curve. The isolation of the individual arteries is often facilitated by sharp dissection of the anterior envelope of peritoneum that invests the greater curvature of the stomach. As the operator moves cephalad, the assistant provides caudad retraction on the stomach to bring the area of interest into better position. Care must be taken, however, not to avulse the short gastric arteries from the undersurface of the spleen. The uppermost short gastric arteries provide a significant technical challenge, but with experience and care, injury to the splenic capsule will be avoided. Metallic clips have been suggested in place of ligatures on the difficult short gastric arteries. The later manipulation in the region, however, may lead to the displacement of the hemostatic clips. Therefore, if possible, well-placed ligatures are desirable. Small capsular injuries to the spleen have been controlled by the application of microfibrillar collagen and gentle pressure. Once the entire greater curvature is free, a pack is placed between the stomach and the spleen in order to prevent splenic injury later in the operation.

A suitable opening is then made along the lesser curve of the stomach in order to introduce the anvil of the TA-90 stapler. A suitable location is chosen high on the lesser curve 1.5 cm below the gastroesophageal junction, and the peritoneum is gently incised. Using blunt dissection, an

instrument such as a right-angle clamp is introduced from either the anterior or posterior side of the lesser curve under direct vision. The opening is gently enlarged to approximately 1 to 1.5 cm. As previously pointed out,[25] the uppermost branches of the left gastric artery are preserved. A soft rubber No. 24 French whistle-tip catheter is led around the lesser curve and the tip of the anvil of the TA-90 stapler is placed into the lumen of the catheter and led from the lesser curve side to the greater curve behind the stomach. Once in place, the stapler is manipulated in order to form a small gastric pouch which should be less than 60 cc in volume by direct measurement.[1] While the surgeon occludes the gastroesophageal junction, the anesthesiologist fills the Ewald tube until flow resistance occurs. Two double rows of staples are applied and the stomach is not divided. A No. 16 French standard nasogastric sump is then substituted for the Ewald tube within the pouch. Controversy exists as to whether the stomach should be divided to ensure that, should the staple line disrupt, the function of the small pouch would not be lost. By proper preoperative preparation of the patient's dietary habits and slow introduction of solid foods for the first six to eight weeks postoperatively, this risk appears to be minimal. We have no documented cases of disruption of the staple line in our series.

Attention is then turned to the construction of the Roux-en-Y limb. At a suitable distance from the ligament of Treitz, the small bowel is divided, and a standard Roux-en-Y limb is formed. Safe ligation of the mesenteric vessels is ensured by incision of the parietal peritoneum and by transilluminating the mesentery and bluntly dissecting away the fat. The Roux-en-Y limb begins after the first major arcuate vessel with a surprisingly short mobilization to gain the required length to reach the stomach. The procedure can be facilitated by the use of an anastomotic stapler. The limb is then led in an antecolic fashion to the region of the gastric pouch; a retrocolic direction may also be chosen. The limb, which is designed to prevent reflux of bilary and pancreatic secretions into the gastric pouch, is then anastomosed to the lateral portion of the gastric pouch on the greater curve just above the staple line. A side-to-side or end-to-side anastomosis is completely closed, the nasogastric tube, with additional side holes cut to provide suction above and below the anastomosis, is led through the stoma into the jejunal limb. After the anastomosis is closed, it is reinforced with nonabsorbable suture and imbricated to reduce the size of the anastomotic lumen. A No. 20 Maloney dilator is placed alongside the No. 16 nasogastric tube and the anastomosis is closed so that no separation exists between the two tubes. Once the anastomosis is completed, the Maloney dilator is removed and the nasogastric tube is taped in place and marked to ensure its proper position. The completed operation is depicted in Figure 1.

Because of the occasional incidence of delayed stomal functioning, a catheter jejunostomy is usually performed as described by Page.[36] The catheter is introduced several centimeters below the jejunojejunostomy of the Roux-en-Y. At this time, a cholecystectomy is performed if there is gallbladder disease, and a liver biopsy may be performed as indicated. After inspection for suitable hemostasis, the abdomen is closed with buried retention sutures.

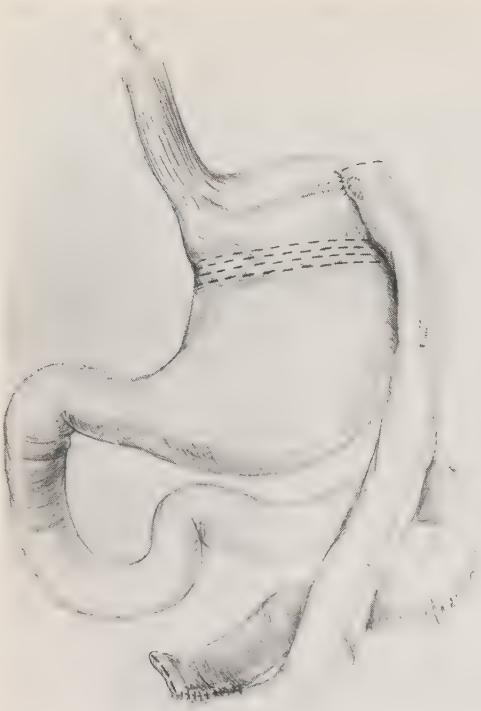

Figure 1. Completed gastric bypass procedure. (Adapted from Maini, B. S., Blackburn, G. L., and McDermott, W. V.: Technical considerations in a gastric bypass operation for morbid obesity. Surg. Gynecol. Obstet., *145*:907, 1977.)

POSTOPERATIVE MANAGEMENT

Patients are not extubated in the operating room (Table 4). Mechanical ventilation is continued in the recovery room until the patient is fully awake and has demonstrated by objective measurements (inspiratory force, forced vital capacity) that extubation is appropriate.[38] If there is any question regarding the patient's capacity for adequate spontaneous ventilation, intubation is continued until the following morning. Once the

Table 4. *Postoperative Procedures*

Intravenous infusions: Maintain carbohydrate-free regimen (*no dextrose*).
No patient should be extubated until in the recovery room.
Nasogastric tube to low suction with gentle (10 cc saline) irrigation.
Irrigate catheter jejunostomy with 10 cc saline every 6 hours.
Urine from Foley—sugar and acetone, specific gravity every 8 hours. Remove Foley as soon as practical.
Keep accurate intake and output records, and weigh patient at least every other day.
Continue mini-heparin dose as preoperatively.
Continue antibiotic for two additional doses only.
Ensure that chest x-ray film confirms the position of the central catheter.
Use nasotracheal suction as needed with low threshold for fever or pulmonary changes.
Schedule upper gastrointestinal series before discharge. Requisition must ask radiologist to *measure volume* of gastric pouch.

patient is extubated, vigorous pulmonary therapy is initiated including incentive spirometry, humidification, physiotherapy, and where necessary, tracheal suctioning. For the same reason, early ambulation is necessary.

Intraoperative and postoperative administration of fluids consists of physiologic electrolyte solutions. Dextrose solutions are not administered so that there will be no interference with the normal metabolic response to injury.[35] By the first postoperative day, the patient has achieved relative hemodynamic stability, and intravenous fluids are then provided in the form of dextrose-free amino acid solutions with the usual electrolyte additives.[9] The absence of significant infection allows the normal development of ketogenesis to partially meet energy requirements. The subsequent ketonemia and ketonuria provide a sensitive indication that there is a relatively normal adaptation to exogenous caloric deficiency. The loss of ketonuria, or the failure to develop ketonuria, should lead to a high index of suspicion of significant infection.[33] Indeed, this metabolic signal may precede by hours the development of other concomitants of invasive sepsis, such as fever and tachycardia.

Recently, Moore et al.[34] and Mason[27] emphasized the importance of the early recognition of an anastomotic leak in reducing immediate postoperative morbidity and mortality. Monitoring of urinary ketones, as well as urinary urea nitrogen,[3] will add additional tools for establishing this diagnosis before irreversible intraperitoneal sepsis is established. Urine samples are obtained each eight to 12 hours for dipstick testing of urinary ketones.

The Foley catheter inserted in the operating room is removed on the first postoperative day or as soon as practical. Mini-dose heparin is resumed in the recovery room and continued until the patient is ready for discharge seven to 10 days after operation. The nasogastric tube is gently irrigated beginning in the recovery room and until its removal. The timing of its removal is based on the usual criteria of return of normal bowel function. Soon after the nasogastric tube is removed, liquids are allowed by mouth in small volume. The diet is advanced as tolerated. The patient is eventually given a specially designed diet for gastric bypass patients with an emphasis on liquids and soft solid food in low volumes.[47]

Approximately one week after operation, each patient has a limited barium upper gastrointestinal series in order to evaluate the bypass procedure. The radiologist carefully attempts to estimate the volume of the pouch based on the amount of barium swallowed, and looks for dysfunction of the anastomosis or the Roux-en-Y loop.

One of the conclusions of the NIH Consensus Conference[46] was that careful follow-up studies of gastric bypass procedures were needed to determine if the weight reduction can be maintained in patients undergoing this operation. It has been correctly observed by Printen that "next to technical expertise in performing the operation, the most important thing is the long-term follow-up of this type of patient."[39] As recently reviewed in the Medical Letter, the gastric bypass appeared to be as effective as the jejunoileal bypass in promoting weight loss and seemed to have fewer long-term complications despite early technical difficulties.[15]

Table 5. *Weight Loss (Pounds) Following Gastric Bypass*

TIME IN MONTHS	MEAN ± S.D.	NO. OF PATIENTS
Preop. weight	303 ± 61	34
1	26 ± 14	27
3	51 ± 17	23
6	75 ± 22	20
12	81 ± 32	11
24	114 ± 31	4
30	104 ± 46	3

RESULTS OF GASTRIC BYPASS

Our own experience as of June 1979 with postoperative weight loss following gastric bypass procedure is indicated on Table 5. These figures resemble other published series. Several years will be needed to chart the ultimate weight loss these patients are able to achieve. Inspection of the data shows that the rate of weight loss begins to slow at approximately one year following operation, but further small weight reduction has been achieved. It will be noted from the weight of the patients one year or more after operation that many patients would still be classified as obese; however, they are now well below 200 per cent of their ideal body weight.

The incidence of early postoperative complications is similar to that reported by other groups.[13, 20, 23, 29] Nausea and some vomiting have been reported by at least two-thirds of our first 40 patients. These symptoms abate as eating habits are modified. One-third to one-half of the patients have minor wound problems, usually consisting of a seroma which does not prolong hospitalization. In one patient a severe wound infection developed leading to dehiscence. There has been one anastomotic leak resulting in death and one fatal pulmonary embolism. The incidence of anastomotic revisions is 5 per cent.

The importance of adequate intake of protein during weight reduction has been repeatedly emphasized. Patients who have undergone gastric

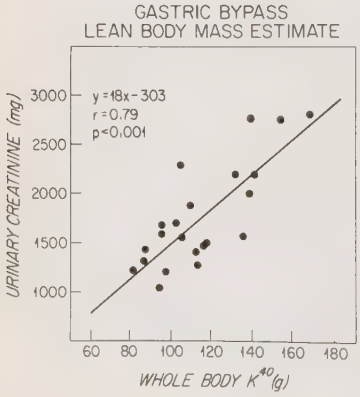

Figure 2. Relationship between whole body potassium-40 and 24-hour urinary urea creatinine as a measure of lean body mass.

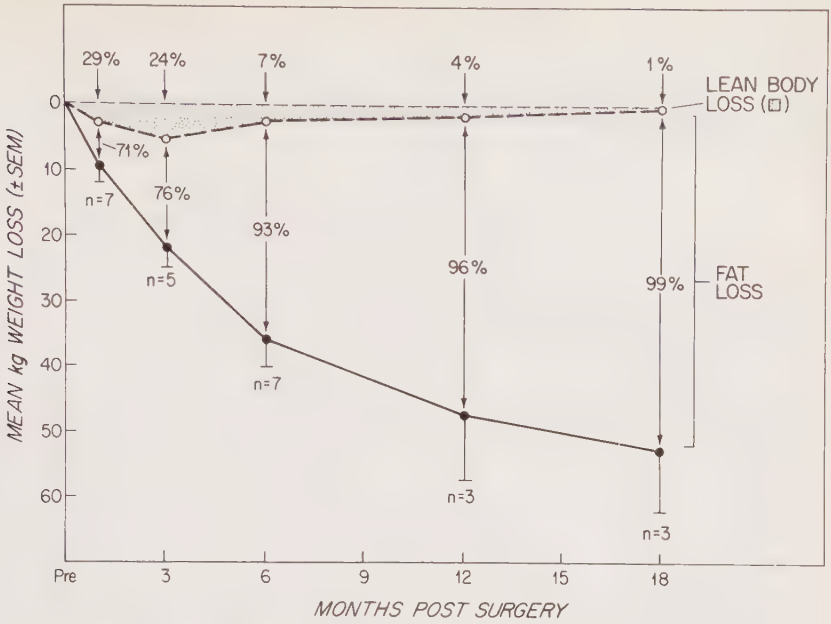

Figure 3. Composition of weight loss following gastric bypass surgery.

bypass are encouraged to consume approximately 1½ gm of protein per kilogram of body weight per day. The changes in lean body mass of a number of patients have been studied by the sensitive techniques of whole body potassium-40[40] and 24-hour urinary creatinine excretion as depicted in Figure 2. The R value of 0.79 suggests that urinary creatinine can serve for the routine follow-up evaluation of these patients in estimating lean body mass.[4] Serial measurements of either potassium-40 or creatinine show the intra-individual error of measurement to be ± 10 per cent. As shown in Figure 3, there is a minimal loss of lean body mass despite ongoing reduction in fat mass. The greatest percentage of total weight loss represented by lean body mass occurred during the first month. The maximal absolute loss of lean body mass appears to have taken place by three months following surgery. Despite continuing fat loss, lean body mass is then gradually restored to the level present preoperatively. This demonstrates that significant weight loss can occur without an obligatory reduction in lean body mass. This experience is distinctly different from that of the jejunoileal bypass procedure in which up to one-third of the early weight loss is from lean tissue.[43]

SUMMARY

Regulation of energy expenditure should be directed toward fat mobilization and oxidation with concomitant preservation of lean body mass. This requires a multidisciplinary approach. The key surgical component of a gastric bypass is a properly sized pouch and stoma outlet.

Compliance with a diet of approximately 800 to 1200 kcal per day, limited to three small meals and two snacks is the desired result. Weight loss should average 10 to 15 pounds monthly when surgery is added to intense medical, nutritional, and behavior therapy to ensure that the weight is reduced to desirable levels.

REFERENCES

1. Alder, R. L., and Terry, B. E.: Measurement of standardization of the pouch in gastric bypass. Surg. Gynecol. Obstet., *144*:763, 1977.
2. Bistrian, B. R.: Clinical use of a protein-sparing modified fast. J.A.M.A., *240*:2299, 1978.
3. Bistrian, B. R.: A simple technique to estimate the severity of stress. Surg. Gynecol. Obstet., *148*:675, 1979.
4. Bistrian, B. R., Blackburn, G. L., et al.: Therapeutic index of nutritional depletion in hospitalized patients. Surg. Gynecol. Obstet., *141*:512, 1975.
5. Bistrian, B. R., Blackburn, G. L., Flatt, J. P., et al.: Nitrogen metabolism and insulin requirements in obese diabetic adults on a protein-sparing modified fast. Diabetes, *25*:494, 1976.
6. Bistrian, B. R., Winterer, J., Blackburn, G. L., et al.: Effect of a protein-sparing diet and brief fast on nitrogen balance in mildly obese subjects. J. Lab. Clin. Med., *89*:1030, 1977.
7. Blackburn, G. L., Bistrian, B. R., Flatt, J. R., et al.: Role of a protein-sparing modified fast in a comprehensive weight reduction program. *In* Howard, A. (ed.): Recent Advances in Obesity Research. London, Newman Publishing, Ltd., 1975.
8. Blackburn, G. L., and Greenberg, I.: Multidisciplinary approach to adult obesity therapy. Int. J. Obesity, *2*:133, 1978.
9. Blackburn, G. L., Hensle, T. E., and Flatt, J. P.: Peripheral amino acid infusions. *In* Fischer, J. E. (ed.): Total Parenteral Nutrition. Boston, Little Brown and Co., 1975.
10. Bray, G.: Obesity in Perspective. NIH Report, 75–78, 1975.
11. Bray, G.: The Obese Patient. Philadelphia, W. B. Saunders Co., 1978, p. 237.
12. Bray, G.: The Obese Patient. Philadelphia, W. B. Saunders Co., 1978, pp. 353–410.
13. Bray, G., Barry, R. E., Benfield, J. R., et al.: Intestinal bypass operation as a treatment for obesity. Ann. Intern. Med., *55*:97, 1976.
14. Buckwalter, J.: Personal communication.
15. Bypass operation for obesity. Med. Lett., *20*:33, 1978.
16. Cranley, J. J., Cranos, A. J., and Sull, W. J.: Diagnosis of deep venous thrombosis by phleborheography. Arch. Surg., *111*:34, 1976.
17. Fried, P. I., McClean, P. A., Phillipson, E. A., et al.: Effect of ketosis on respiratory sensitivity to carbon dioxide in obesity. New Engl. J. Med., *294*:1081, 1976.
18. Greenberg, I., Palumbo, J., and Blackburn, G. L.: Obesity: Facts, fads, and fantasies. Comprehensive Therapy, 1979, In press.
19. Harrison, M. T., Harden, R. M. G.: The long-term value of fasting in the treatment of obesity. Lancet, *2*:1304, 1966.
20. Hermreck, A. S., Jewell, W. R., and Harden, C. A.: Gastric bypass for morbid obesity: Results and complications. Surgery, *80*:498, 1976.
21. Hirsh, J., and Knittle, J. L.: Cellularity of obese and nonobese human adipose tissue. Fed. Proc., *29*:1516, 1970.
22. Hofman, A. F., Northfield, T. C., and Thistle J. L.: Can a cholesterol-lowering diet cause gallstones? New Engl. J. Med., *288*:46, 1973.
23. LaFave, J. W., and Alden, J. F.: Gastric bypass in the operative revision of the failed jejunoileal bypass. Arch. Surg., *114*:438, 1979.
24. Maini, B. S.: Surgical approaches. *In* Blackburn, G. L. (ed.): Obesity. Boston, Center for Nutritional Research, 1977.
25. Maini, B. S., Blackburn, G. L., and McDermott, W. V.: Technical considerations in a gastric bypass operation for morbid obesity. Surg. Gynecol. Obstet., *145*:907, 1977.
26. Mason, E. E.: Personal communication.
27. Mason, E. E.: Surgical pros and cons. Surg. Gynecol. Obstet., *148*:765, 1979.
28. Mason, E. E., and Ito, C.: Gastric bypass in obesity. SURG. CLIN. NORTH AM., *47*:1345, 1967.
29. Mason, E. E., Printen, F. J., Hartford, C. E., et al.: Optimizing results of gastric bypass. Ann. Surg., *182*:405, 1975.
30. McGovern, G.: Hearings Before the Select Committee on Nutrition and Human Needs of the U.S. Senate. Washington, D.C., U.S. Government Printing Office, 1973.

31. McGovern, G.: Hearings Before the Select Committee on Nutrition and Human Needs of the U.S. Senate, Part 2, Obesity. Washington, D.C., U.S. Government Printing Office, 1977.
32. Metropolitan Life Insurance Company, 1960.
33. Miller, J. D. B., Blackburn, G. L., Bistrian, B. R., et al.: Effect of deep surgical sepsis on protein-sparing therapies and nitrogen balance. Am. J. Clin. Nutr., *30*:1528, 1977.
34. Moore, E. E. Buerk, C., and Moore, G.: Surgical pros and cons. Surg. Gynecol. Obstet., *148*:764, 1979.
35. Page, J. G., Blackburn, G. L., et al.: Crystalloid therapy in resuscitation during routine surgery and severe trauma. Surg. Forum, *26*:18, 1975.
36. Page, C. P., Ryan, J. A., Jr., and Haff, J. C.: Continual catheter administration of an elemental diet. Surg. Gynecol. Obstet., *142*:184, 1976.
37. Pomerantz, A. S., Greenberg, I., and Blackburn, G. L.: MMPI profiles of obese men and women. Psychol. Rep., *41*:731, 1977.
38. Pontoppidan, H., Geffin, B., and Louwenstein, B.: Acute respiratory failure in the adult. New Engl. J. Med., *287*:690, 799, 1972.
39. Printen, K. J.: Discussion of gastric bypass for morbid obesity. Surgery, *80*:503, 1976.
40. Shizgal, H. M.: Total body potassium and nutritional status. SURG. CLIN. NORTH AM., *56*:1185, 1978.
41. Sigler, M. H.: The mechanism of the natriuresis of fasting. J. Clin. Invest., *55*:377, 1975.
42. Skinner, D. B. and Salzman, E. W.: Anticoagulant prophylaxis in surgical patients. Surg. Gynecol. Obstet., *125*:741, 1967.
43. Spainer, A. H., Kurtz. R. S., Shilata, H. R., et al.: Alterations in body composition following intestinal bypass for morbid obesity. Surgery, *80*:171, 1976.
44. Stunkard, A. and McLaren-Hume, M.: Results of treatment of obesity. Arch. Intern. Med., *103*:79, 1959.
45. Tullis, J. L.: Clot. Springfield, Ill., Charles C Thomas, 1976, pp. 408–409.
46. Van Itallie, T. B., and Burton, B. T.: National Institutes of Health Consensus Development Conference on Surgical Treatment of Morbid Obesity. Ann. Surg., *189*:455, 1979.
47. Wade, J., and Blackburn, G. L.: Dietary guidelines for patients following gastric bypass. Boston, New England Deaconess Hospital Diet Manual, 1979.

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Surgical Experience with Jejunoileal Bypass for Morbid Obesity

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A surgical approach to massive, exogenous (morbid) obesity is based on the dual concept that it is a serious, life-shortening disorder and that medical treatment is usually unsuccessful.[6, 7] Various operative procedures have been suggested, but extensive jejunoileal bypass has been used most widely.

In the last 12 years we have made a clinical, psychologic, and metabolic study of morbid obesity and the effects of jejunoileal bypass in management of 225 patients. Patients were selected for operation from a much larger group after appraisal of their clinical and metabolic status. Criteria for selection included: obesity of at least two to three times ideal weight of 10 to 15 years' duration; evidence from both history and attending physician of failure of dietary management over a period of years; absence of correctable endocrinopathy (hypothyroidism, Cushing's syndrome); absence of unrelated significant disease which might increase operative risk; presence of complications such as Pickwickian syndrome, hyperlipidemia, and adult onset of diabetes or hypertension which might be alleviated by obligatory weight loss; and assurance of the patient's cooperation in prolonged follow-up.[10, 12]

CLINICAL APPRAISAL

The end-to-side jejunoileal shunt described by Payne[6, 7] was used in 11 early patients, but inadequate weight reduction in these led us to the use of end-to-end jejunoileal shunt with drainage of the bypassed small bowel into the colon in 214 patients (Fig. 1).

There were 135 women and 90 men in the group, whose ages ranged from 16 to 63 years, with an average of 36 years. Weights ranged from 110 to 186 kg in women, with an average of 137 kg; in men, weights ranged from 123 to 255 kg, with an average of 174 kg.

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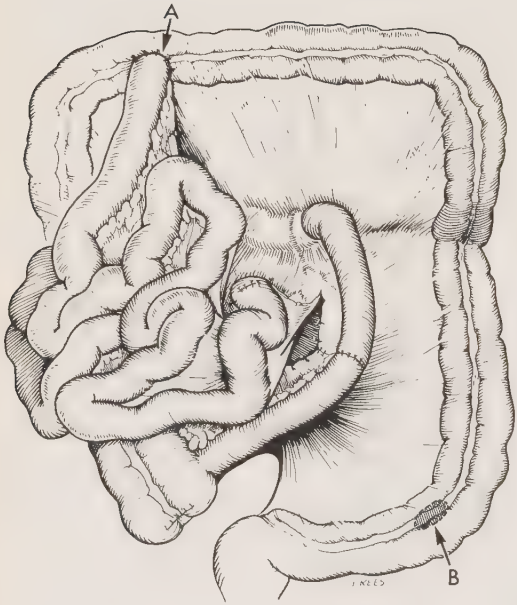

Figure 1. The technique of end-to-end jejunoileostomy with extensive jejunoileal bypass. The closed end of the bypassed jejunum is sutured securely to the mesentery to prevent intussusception. The end of the bypassed ileum is drained by end-to-side anastomosis with the transverse colon (A) or sigmoid (B).

Table 1. *Additional Findings in 225 Patients with Morbid Obesity*

Hyperlipidemia	112
Gallstones	62
Diabetes	49
Hypertension	31
Incisional or umbilical hernia	19
Gout	13
Ovarian cyst	9
Pickwickian syndrome	8
Hiatal hernia with reflux	4
Fibroids of uterus	3
Carcinoma of uterus	3
Carcinoid of intestine	2
Peptic ulcer (inactive)	2
Carcinoma of cervix	1
Carcinoma (male) breast	1
Abdominal aortic aneurysm	1
Angina pectoris	1
Myocardial infarction (old)	1
Osteomyelitis of tibia (old)	1

Table 1 summarizes the additional findings prior to operation in these obese patients. One hundred and twelve (50 per cent) of the group had hyperlipidemia, most frequently type IV hyperlipoproteinemia, and less frequently familial hypercholesterolemia (types IIa and b). Gallstones (27 per cent), adult onset diabetes (22 per cent), and hypertension (14 per cent) were other rather frequent findings. Aside from diabetes, no endocrinopathy was identified in these patients. Except as in Table 1, preoperative absorptive status, gastrointestinal radiography, vitamin levels, and hematologic studies were normal.

OPERATION

A three to five day cleansing bowel preparation was used in each patient with oral neomycin and tetracycline for 36 hours prior to operation. Early in our experience halothane was used for anesthesia but in recent years "balanced anesthesia" has been used. A transverse epigastric incision which transected both recti was used in most patients.

Figure 2 shows diagrams of the four modifications of jejunoileal bypass used in this study. The dimensions are in centimeters. All patients survived the operation, but five patients died from postoperative complications (Table 2). The operative mortality rate was 2.2 per cent.

Most patients had an uneventful recovery from the operation, although nonfatal postoperative complications developed in 49 (22 per cent). These included wound seroma (14 patients) and superficial wound infection (15 patients). One of the latter also developed stomal obstruction which required revision and venous thrombosis with pulmonary emboli.

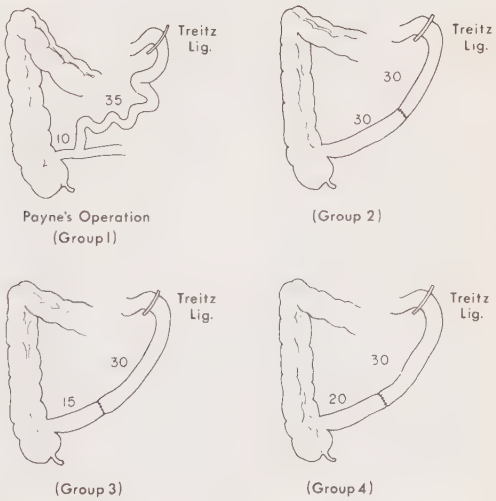

Figure 2. The four modifications of jejunoileal bypass used in this study (measurements are in centimeters).

Table 2. *Operative Mortality in 225 Patients with Morbid Obesity*

Pulmonary embolism	3
Thrombophlebitis, sepsis, hemorrhagic pneumonitis	1
Infarction of ileum after resection of carcinoid	1
TOTAL	5 (2.2 per cent)

Twelve other patients had thromboembolic complications. There were five urinary tract infections and one evisceration. All of these patients recovered with appropriate treatment.

Before discharge from the hospital (usually eight to ten days after operation) each patient was instructed in the importance of control of diarrhea to no more than three to four liquid stools per day by adhering to a high protein low fat diet and the use of antidiarrheal drugs. In recent years instruction in a low oxalate diet has been added to reduce the potential of urinary stones.

FOLLOW-UP STUDIES AND RESULTS

Although early precipitant weight loss occurred in each group, those with end-to-side jejunoileal shunt (Group 1) and those with 30 cm to 30 cm end-to-end jejunoileal shunt (Group 2) began to regain weight after 12 to 18 months. Weights were most effectively reduced and the reductions best sustained in Groups 3 and 4 which had the shortest lengths of in-continuity small intestine (45 cm) (Fig. 3). More than 70 per cent of patients in Groups 3 and 4 followed for one or more years achieved weight reduction to the "ideal" range.

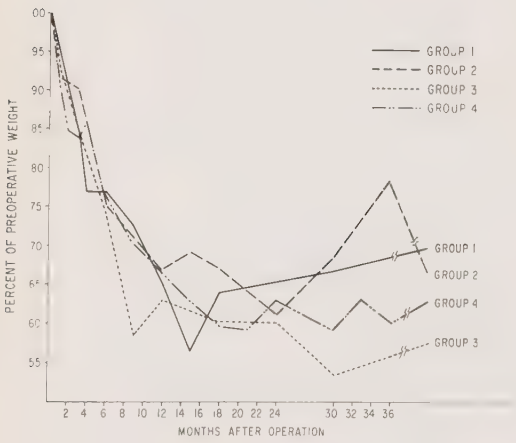

Figure 3. Body weight after jejunoileal bypass as a percentage of preoperative weight.

Metabolic parameters which were assessed prior to operation have been restudied during follow-up.[10] A reduction in carbohydrate absorption was measured by impairment of d-xylose tolerance and flattening of oral glucose tolerance curves. This is reflected clinically by the fact that no diabetic patient has required insulin or tolbutamide since operation.

Malabsorption of fat and interference with enterohepatic cycles of cholesterol and bile acids have been accompanied by an impressive and sustained fall in serum cholesterol and triglycerides in all groups (Fig. 4). After jejunoileal bypass the reduction in serum cholesterol and triglyceride does not tend to rise during follow-up (Fig. 5).[9]

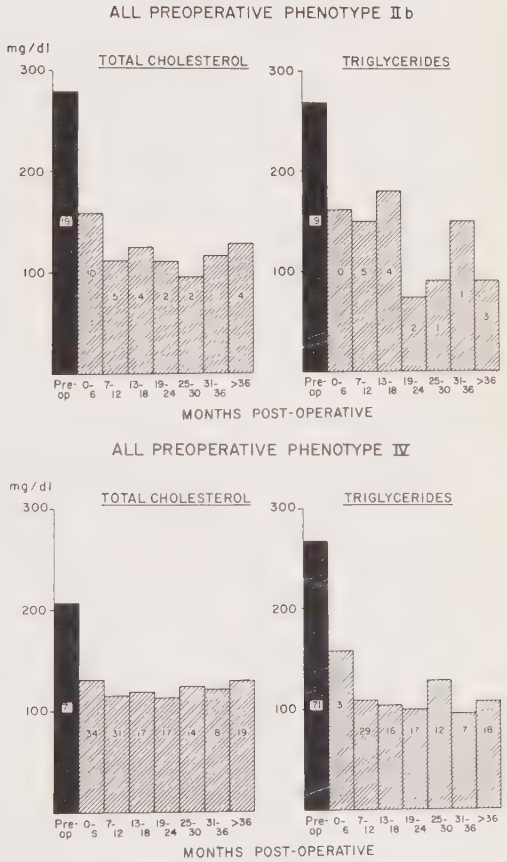

Figure 4. Alterations in mean serum cholesterol and triglyceride concentrations in morbidly obese patients after jejunoileal bypass.

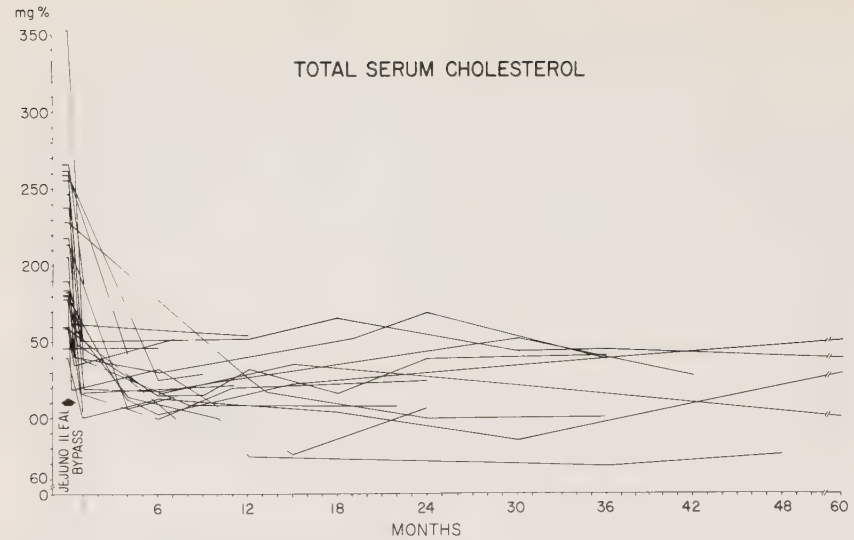

Figure 5. After jejunoileal bypass, the reduction in serum cholesterol and triglyceride does not tend to rise during follow-up.

Results of studies of body composition after jejunoileal bypass indicate that both body fat and lean tissue are lost in the early months after operation. In all groups potassium homeostasis was usually achieved after four to six months and subsequently fat was lost in preference to lean tissue.[8]

Metabolic complications after jejunoileal bypass have included hyperoxaluria with urinary stones, the enterohepatic syndrome of hepatocellular injury secondary to heavy bacterial growth in the bypassed bowel, electrolyte and acid-base alterations secondary to persistent diarrhea, hyperuricemia and gouty arthritis, vitamin deficiencies, and manifestations of various other malabsorptive syndromes. In approximately 15 per cent of patients, clinical and laboratory evidence was found of the enterohepatic syndrome, and a similar frequency of one or more oxalate urinary stones has been observed.

During the follow-up period from 1966 to 1979 in the 220 patients who survived operation, 11 deaths have occurred, five of which were unrelated to jejunoileal bypass. In five patients, however, fatal hepatic failure occurred, and one patient died from renal failure and stress gastric bleeding secondary to uncontrolled diarrhea.

Follow-up results have been appraised critically in all surviving patients in each group who have been observed for one year or longer after operation. These are summarized in Table 3. In Groups 1 and 2 good results were achieved in only four of 21 patients. Except for one patient who died from alcoholic cirrhosis, fair and poor results in Groups 1 and 2 can be credited to inadequate weight loss. In groups 3 and 4 good results were achieved in 130 of 175 patients (75 per cent). Fair and poor results in these groups, as well as the six related deaths which have been listed,

Table 3. *Results of Follow-Up of 196 Patients Who Underwent Jejunoileal Bypass for Obesity from 1966 to 1978 at Vanderbilt University*

END-TO-SIDE JEJUNOILEAL SHUNT	NUMBER OF PATIENTS	YEARS	RESULTS		
			Good	Fair	Poor
Group 1: Payne Procedure, 35 to 10 cm	11	8 to 11	0	1	10
Group 2: 30 to 30 cm	10	7 to 8	4	2	5
Group 3: 30 to 15 cm	19	6 to 7	13	4	2
Group 4: 30 to 20 cm and 25 to 20 cm	156	1 to 6	117	23	16

were usually a result of metabolic complications rather than of poor weight control.

COMMENT

The degree of rehabilitation in the patients who have had good results from jejunoileal bypass and in most of those who have had fair results is difficult to measure objectively. Return to full preoperative work capacity or assumption of new work has been accomplished by all but 15 patients in the good and fair categories. In the latter small group retirement programs or wealth which precluded the need to work are important influences. The new body image developed by those who have achieved reductions to a normal or near normal weight range has been impressive to our surgical group and in particular to our clinical psychologists and psychiatric consultants. Psychologic studies have been reported separately.[1, 13]

In recent years we have used the 12 to 18 inch (30 to 20 cm) end-to-end jejunoileal shunt in most obese patients whose weights are in the range of 350 pounds (160 kg) or less, and have reserved the 12 to 6 inch (30 to 15 cm) or 10 to 8 inch (25 to 15 cm) end-to-end jejunoileal shunt for massively obese patients whose weights are in excess of 350 pounds (160 kg).

The metabolic complications of greatest frequency (15 per cent) and importance after jejunoileal bypass for obesity are "bypass enteritis" or, as we prefer to call it, the "enterohepatic syndrome" of hepatocellular injury from heavy bacterial growth in the bypassed small bowel, and hyperoxaluria and oxalate urinary stones.[2, 3, 5]

The enhanced fatty metamorphosis of the liver coupled with protein-calorie malnutrition which occurs after jejunoileal bypass resembles an adult form of the tropical protein deficiency disorder known as kwashiorkor. Our clinical metabolic and body compositional data support the concept that the majority of massively obese patients treated by jejunoileal bypass will recover from this phase of protein depletion and hepatic fatty metamorphosis in an entirely satisfactory manner if no added hepatotoxic factors are imposed. Excessive alcohol intake after jejunoileal bypass

clearly led to alcoholic hepatosis, necessitating revision of the shunt in two patients, and cirrhosis, variceal hemorrhage, and death from hepatic failure in two others. We believe alcohol abuse was contributory to the similar death from hepatic failure in one other patient. We advise all patients to abstain from alcohol after a jejunoileal bypass.

Another possible cause of hepatic injury after jejunoileal bypass is the potential of bacterial colonization and overgrowth in the bypassed jejunoileum with toxic absorption of bacterial metabolites, deconjugates such as lithocholic acid, or bacterial endotoxin. The experimental work of Woodward et al.[2, 5] and our own studies[4, 11] support this possibility and suggest the use of broad spectrum antibiotic therapy.

Close clinical observation of all patients who undergo jejunoileal bypass is mandated by the uncommon but hazardous potential for development of toxic damage to the liver, especially during the transient phase of protein-calorie malnutrition. The clinical symptoms are those of a flulike syndrome of malaise, myalgia, weakness, and easy fatigue coupled with anorexia and nausea. Elevation of serum alkaline phosphatase, lactic dehydrogenases, and serum glutamic-oxalacetic transaminase values usually precede a rise in the bilirubin level or clinical jaundice. Australia antigen is usually negative. In most patients in the present series in whom these clinical manifestations developed within a few weeks to 18 months after jejunoileal bypass, treatment for three to four weeks with Flagyl (metronidazole), tetracyclines, or doxycycline, coupled with elemental dietary supplements, has resulted in a subsidence of symptoms, a reversal of the serum enzyme alterations, and a return of biopsies to normal. Failure of prompt response to such treatment is an indication for revision of the intestinal bypass and the restoration of continuity of the alimentary tract.[3, 11]

Hyperoxaluria and one or more oxalate urinary stones have occurred in 15 per cent of patients in this series. The problem seems to be most closely related to the shortened bowel and the preferential binding of available calcium in the colon by free bile acids, thus permitting unbound oxalic acid to be absorbed in excess and excreted in urine. Excess oxalate and fat in the diet exaggerate the problem by further binding calcium to fatty acids. Hyperoxaluria is then the basis for formation of calcium oxalate stones. In recent years all patients in this series have been instructed to follow a high protein, low fat, low oxalate diet. This has reduced but by no means eliminated this complication of the short bowel syndrome.[3, 14]

The large reduction in serum lipid concentrations as well as the large reduction in body fat that results from jejunoileal bypass should be of value in slowing the progress of atherogenesis and its catastrophic manifestations in these obese patients.[3, 9]

Long-range clinical, metabolic and nutritional follow-up study is mandatory and is best conducted by the operating surgeon.

SUMMARY

Jejunoileal bypass for morbid obesity with our current bowel length

dimensional considerations has achieved good results in 74 per cent of patients. Morbidity and mortality are significant and must limit wide application of the procedure.

REFERENCES

1. Abram, H. S., Meixel, S. A., Webb, W. W., et al.: Psychologic adaptation to jejunoileal bypass for morbid obesity. J. Nerv. Ment. Dis., *162*:151, 1976.
2. Brown, R. G., O'Leary, J. P., and Woodward, E. R.: Hepatic effects of jejunoileal bypass for morbid obesity. Am. J. Surg., *127*:53, 1974.
3. Buchwald, H., Varco, R. L., Moore, R. B., et al.: Intestinal Bypass Procedures. Chicago, Year Book Medical Publishers, 1975.
4. Edmiston, C. E., Jr., Hulsey, T. K., Scott, H. W., Jr., et al.: Microbial colonization and hepatic abnormalities in jejunoileal bypass. J. Infect. Dis., 1979, in press.
5. O'Leary, J. P., Maher, J. W., Hollenbeck, J. I., et al.: Pathogenesis of hepatic failure after jejunoileal bypass. Surg. Forum, 25:356, 1974.
6. Payne, J. H., and DeWind, L. T.: Surgical treatment of obesity. Am. J. Surg., *118*:141, 1969.
7. Payne, J. H., DeWind, L. T., Schwab, C. E., et al.: Surgical treatment of morbid obesity. Arch. Surg., *106*:432, 1973.
8. Scott, H. W., Jr., Brill, A. B., and Price, R. R.: Body composition in morbidly obese patients before and after jejunoileal bypass. Ann. Surg., *182*:395, 1975.
9. Scott, H. W., Jr., Dean, R. H., LeQuire, V., et al.: Alterations in plasma lipid concentrations in normal and hyperlipidemic patients with morbid obesity before and after jejunoileal bypass. Am. J. Surg., *135*:341, 1978.
10. Scott, H. W., Jr., Dean, R., Shull, H. J., et al.: New considerations in use of jejunoileal bypass in patients with morbid obesity. Ann. Surg., *177*:723, 1973.
11. Scott, H. W., Jr., Dean, R. H., Shull, H. J., et al.: The results of jejunoileal bypass in 200 patients with morbid obesity. Surg. Gynecol. Obstet., *145*:661, 1977.
12. Scott, H. W., Jr., Law, D. H., IV, Sandstead, H. H., et al.: Jejunoileal shunt in surgical treatment of morbid obesity. Ann. Surg., *171*:770, 1970.
13. Webb, W. W., Phares, R., Abram, H. S., et al.: Jejunoileal bypass procedures in morbid obesity: Preoperative psychological findings. J. Clin. Psychol., 32:82, 1976.
14. Wright, H. K., and Tilson, M. D.: The Short Gut Syndrome: Pathophysiology and Treatment. Chicago, Year Book Medical Publishers, 1971.

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The Control of Food Intake: Effects of Dieting and Intestinal Bypass

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Intestinal bypass has provided an opportunity to study the factors which modify food intake in human beings. Although a number of investigators have contributed to the study of this area,[6, 15–16, 20, 25–26, 40, 43] the following discussion will focus primarily on data obtained from our studies with overweight individuals who have undergone intestinal bypass surgery.[2–4, 6–10, 12, 14–20, 24, 27–28, 45] Although a number of factors influence the rate and magnitude of weight loss, including the initial length of the intestine,[5, 8, 34] the length of the segment remaining in continuity,[8, 39, 42, 53] the type of operation,[51] the initial body weight,[5, 8, 40] the amount of food eaten,[6, 15–16, 25–26, 40, 43] and the degree of malabsorption, weight loss after intestinal bypass results primarily from a decrease in food intake rather than from malabsorption.[9–10, 15–16, 19–20]

Evidence for Decreased Food Intake After Bypass

Following intestinal bypass, food intake decreases in most, if not all, patients, a finding which has now been reported by several groups of investigators.[6, 15–16, 20, 25–26, 40, 43] In our first group of patients, preoperative energy intake averaged 6700 calories a day. During the first six months after surgery, there was a marked drop to values below 2000 calories per day in many patients.[9–10, 15] Over the ensuing months following surgery, a gradual increase in food intake occurred, but it never returned to

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preoperative levels. These retrospective data on food intake have been accompanied by measurements of food intake during an ad libitum feeding situation in the hospital both before and after surgery.[6, 18] Estimates of caloric intake are shown in Figure 1. For these measurements, subjects were fed more food than they requested, and the difference between the quantity of food available and the amount eaten during these two meals was measured. Using data on 21 of our patients in whom such measurements were obtained, weight loss and the decrease in caloric intake after jejunoileal bypass showed a significant correlation ($r = .52$, $p < .05$).[18]

The pattern of food intake also changed,[18, 40] and the quantities of food eaten at individual meals rose. Preoperatively, only 15 per cent of the food was eaten at breakfast, compared with 30 per cent during this time interval postoperatively.[18] A similar and marked shift was noted in nighttime eating where 25 per cent of calories were consumed in this period preoperatively but only 10 per cent in the postoperative period.[18]

Reduction in the quantity of food eaten has also been estimated by using liquid formula diets and measuring cumulative intake of liquids over a 20 minute meal time.[6, 16, 18] The chocolate-flavored liquid formula used for these studies was chilled and available to the subjects through a straw in a concealed container. The weight of the container was recorded every two minutes for 20 minutes, and the total intake before and after surgery was measured on five separate days. The intake for one individual is recorded in Figure 2.

Accompanying the decline in meal size, there was an increase in the sensitivity of the obese individuals to a caloric preload. For this study, each subject received, on a different day, a milkshake containing either 200 or 440 kcal. These milkshakes had been disguised so that by taste alone, the changes in caloric content could not be distinguished. Half an hour after drinking the milkshake, a standard meal was provided and the amount of food eaten was recorded. These data have been summarized in Figure 3. Before surgery, the caloric intake from the test meal was nearly twice as high as postoperatively, and the differences between caloric preloads was not statistically significant. Postoperatively, however, the number of calories eaten after the 440 calorie preload was significantly less than with the 200 kcal preload[15, 16] using a paired "t" test.

Intestinal bypass also modifies taste preferences for high concentrations of sucrose and glucose.[15, 16, 45] Patients were given increasing concentrations of glucose solution in a double-blind fashion and were asked to rate them for pleasantness and intensity. In terms of intensity, the subjects detected and successfully scaled the increasing concentration of glucose, and the ratings before and after surgery remained virtually unchanged. However, the ratings for pleasantness of taste revealed significant changes after surgery. Preoperatively, the pleasantness ratings for glucose were variable with no consistent pattern. After surgery, the preference for glucose showed a maximum rating at a concentration of one molar and then declined. There were no reliable correlations between the preoperative and postoperative ratings for lower or higher concentrations. Similar effects were observed with solutions

Study	Calories Eaten*	
	Before Surgery	After Surgery
1	4766±259	2965±194
2	2963±393	1392±251

*Data in Study 1 were obtained from the morning and evening meal; the data in Study 2 from the mid-day meal.

Figure 1. Caloric intake before and after intestinal bypass.

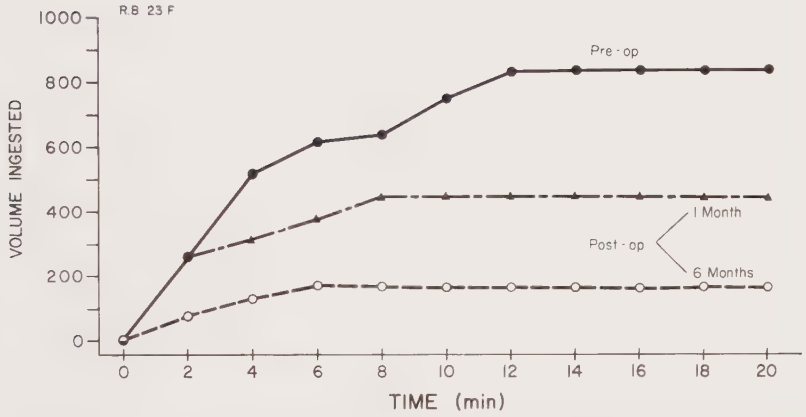

Figure 2. Average cumulative liquid intake over a 20 minute meal time with a liquid formula diet. The intake at one and six months after operation is significantly less than preoperatively.

Preload (kcal)	Caloric Intake (kcal)	
	Before Surgery	After Surgery
440	1284±99*	651±103
200	1375±99	757± 84
P	N.S.	<.05

*Mean±SEM.

Figure 3. Effect of a preload on caloric intake before and after bypass surgery.

containing different concentrations of sucrose.[15, 16] The 2.5, 5, 10 and 20 per cent solutions of sucrose produced the same ratings before and after surgery. However, the 40 per cent solution of sucrose was significantly less pleasant for the obese subjects after surgery than before (Fig. 4).

Mechanisms for Decreased Food Intake

Several mechanisms might account for the alterations in taste preferences, for the reduced caloric intake, and for the improved sensitivity to caloric preloads following intestinal bypass. The present discussion will focus on the physiologic mechanisms for disposal of food and the potential control mechanisms which may be involved in this system. As a point of reference, a simple scheme has been presented in Figure 5. The control elements in the central nervous system are shown in the upper left hand corner. The oral components are to the right. Below are the intestinal and postingestional components. The effects associated with energy expenditure, and an energy storage system are also to be noted. One or more of these various components may signal to the neural control system to terminate eating or prolong the interval before the next meal or both. Since the major effects of intestinal bypass in man[6, 18] and in animals[50] appear to be a reduction in meal size as well as an alteration in the pattern of eating,[18, 40] it appears appropriate to examine the possible sites for feedback information which may terminate eating.

Table 1 shows the sites at which signals may be generated for terminating feeding, and lists the potential signals for this process. There are three main groups. The oral cavity with its sensory organs for taste and smell may be affected by sensory information about the quality of food being ingested. One might anticipate that mechanisms producing alterations in taste and smell would alter feeding. The changes in taste for glucose and sucrose observed after intestinal bypass[16, 45] may thus be one important mechanism by which the alteration in food intake occurs. After bypass, both zinc and copper are reduced.[3] Since zinc depletion has been shown to produce alterations in taste and decreased food intake both experimentally and clinically,[13] the loss of zinc which occurs following an intestinal bypass may be an important mechanism for the changes.

Table 1. *Factors Which May Reduce Food Intake*

SITE OF GENERATION OF SIGNAL	POSSIBLE SIGNALS FOR A REDUCTION IN FOOD INTAKE
Oral	Chemical (taste, smell)
Gastrointestinal	Mechanical distention
	Nutrients (chemical)
	Direct (glucose, fatty acids, or amino acids)
	Indirect (cholecystokinin, gastrin, entero-glucagon, neurotensin)
Postingestional	Nutrients (glucose, fatty acids, glycerol, amino acids, micronutrients, chylomicrons)
	Hormones (insulin, glucagon, pancreatic polypeptide, steroids, growth hormone)

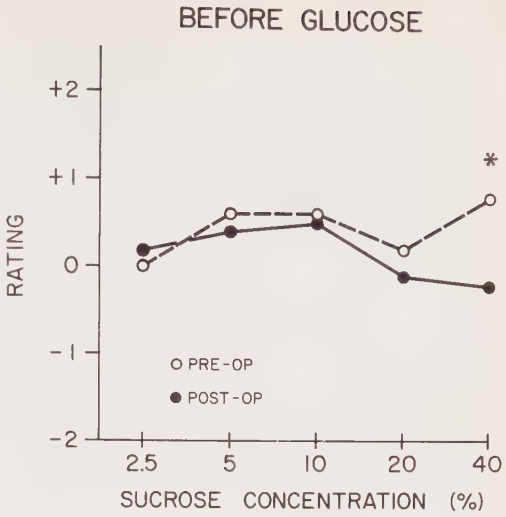

Figure 4. Effect of intestinal bypass on preference for sucrose. After surgery the preference for a 40 per cent solution of sucrose was significantly reduced. A load of glucose of 50 gm did not change the effect of surgery on ratings for sucrose.

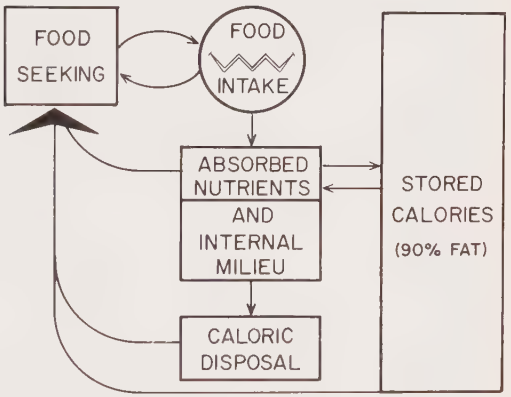

Figure 5. Diagram of food intake and energy stores. The food seeking components are located in the brain. The food intake refers to taste and gastrointestinal tract. Absorbed, stored, and utilized calories are the other components.

Gastrointestinal factors associated with the control of feeding may involve both mechanical distention and nutrient composition of the food which is ingested. The effects of mechanical distention have been clearly demonstrated in experimental studies,[35] and may also be important after bypass. Increased awareness of gastrointestinal filling has been noted in our patients.[21] They also experience episodes of bloating and abdominal distention which may heighten their awareness of food in the gastrointestinal tract.[7] Bacterial overgrowth may also be a factor in the intestinal distention and abdominal awareness.[7, 24]

The number of calories eaten seems to be of major long-term importance[16] and appears to overshadow distention.[35] The nutrient composition of a meal may produce feedback signals directly through the concentrations of glucose, fatty acids, monoglycerides, glycerol, amino acid, or micronutrients.[13] Conversely, nutrients may produce their effects indirectly by alterations in the secretion of various intestinal hormones.[52]

Such hormones may operate by slowing gastrointestinal emptying and thus producing mechanical distention or changing the rate of intestinal motility, and may also have their effects in the systemic circulation. Among the gastrointestinal hormones which must be considered in this connection are cholecystokinin, gastrin, enteroglucagon, neurotensin, and possibly others.[17]

Postingestional factors may also be of importance in terminating feeding. Nutrients crossing the intestinal tract must be considered as well as hormones. Glucose, glycerol, short chain fatty acids, amino acids, and micronutrients all enter the portal circulation for transit to the liver. Long chain fatty acids are repackaged into chylomicrons within the intestinal luminal cells, and released into the lacteals and eventually into the peripheral circulation, thus circumventing the liver. In addition to these nutrients, there are a number of hormones whose concentrations may modulate feeding. Insulin, glucagon, pancreatic polypeptide, steroid hormones, and growth hormone may all play a role in the control of feeding.[11]

Clinical Studies

To define some of the metabolic correlates by which intestinal bypass might produce a change in feeding behavior, we examined a group of patients in whom weight loss was achieved by two methods, first by dieting, and then by intestinal bypass.[17, 28] Each patient was studied on three occasions. The first study was carried out at the time of admission to the hospital. This was followed by a second study performed after a weight loss which averaged 8.5 and 9.5 kg for the four women and three men, respectively. A third study was performed following intestinal bypass in which an attempt was made to achieve comparable degrees of weight loss. This goal was met for the women, whose weight loss averaged 10.1 kg, but was not achieved for the men, whose weight loss averaged 28 kg (Fig. 6).

Voluntary food intake was significantly reduced by bypass but not after dieting (Table 2). Gastric emptying was slower after bypass although this difference was not significant. The value after bypass was comparable to the rate of gastric emptying seen in normal weight controls (Table 3).

In addition to the reduction in food intake noted above we found perceptual changes including a reversible form of depression. We have also detected several metabolic differences between dieting and intestinal bypass.[17]

Comparison of the perceptual changes that occurred in the same individuals before and after relatively similar amounts of weight were lost by dieting and jejunoileostomy provided a way to separate the effects of weight loss per se from those of bypass.

First, it is important to consider those perceptual factors that did not change. Neither dieting nor bypass led to changes in responsiveness to environmental stimuli. Thus, after both procedures, individuals who are highly responsive to external cues remain vulnerable to the influence of salient and palatable food cues. However, apparent benefits obtained

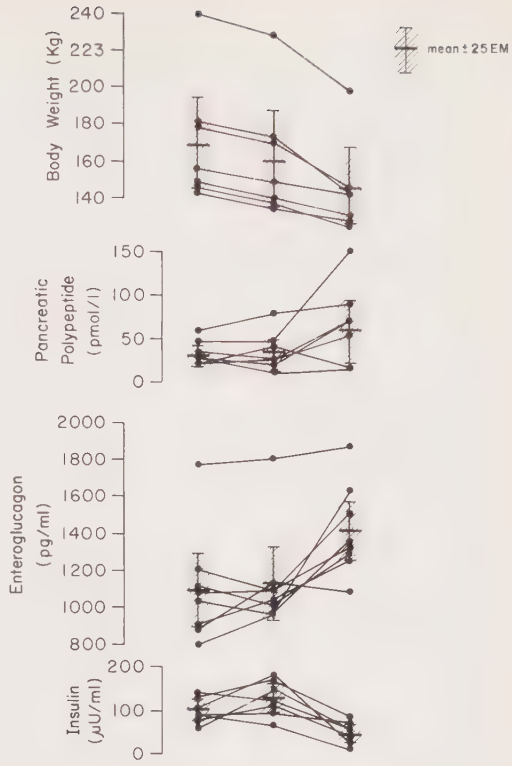

Figure 6. Effect of dieting and intestinal bypass on three hormones. Preoperative measurements of insulin, enteroglucagon, and pancreatic polypeptide are shown on the left. The effects of dieting are shown in the middle and data after bypass are presented on the right.

Table 2. *Gastric Emptying*

		Half-time for Gastric Emptying ($t_{1/2}$ in min)
Normal	6	54.0±7.7
Obese	6	
Before		41.7±5.6
After		50.8±5.9

Table 3. *Summary of Hormonal and Metabolic Changes After Intestinal Bypass*

	Before Treatment	After Dieting	After Bypass	P
I. Hormonal				
Insulin (μU/ml)	30±3	40±5	18±3	<.01
Glucagon (pg/ml)	148±37	142±37	155±31	N.S.
Enteroglucagon (pg/ml)	933±92	904±84	1085±100	<.05
Pancreatic polypeptide (pg/ml)	10.5±2.0	10.2±1.7	16.5±4.1	<.05
Gastrin	160±10	160±11	200±20	<.05
II. Metabolites				
Glycerol	0.041±.009	.038±.008	.058±.009	<.05
Glucose (mg/dl)	90±3	85±3	83±1	<.01
Copper (μg/ml)	147±10	-	90±5	<.01
Zinc (μg/dl)	76±3	-	62±2	<.01

from the bypass and not from dieting, such as reduced preference for sweets, increased experience of satiety, and fewer food cravings, may counteract this external tendency to some extent and thus work to reduce food intake.

Other studies have reported increased distortions in time perception and body image after dieting,[31-33] but we found no change in these two measures. Bypass has also been reported to increase the accuracy of body size estimation but leave the affective component of body image unchanged.[22, 48] Again, our subjects showed no significant change in body perception after bypass. As noted in a recent review,[29] procedures for measuring perceived body size and body image vary so greatly that the inconsistent findings from study to study appearing in the literature are not surprising.

The type of weight loss procedure greatly influenced the affective state of almost all the patients, as indicated by ratings of depression and emotional state.[17] On many measures the bypass procedure was significantly better than dieting, thus suggesting that it is not weight loss per se but weight loss due to dieting deprivation that is related to negative affect. This occurs despite the physical discomfort associated with bypass surgery and it is possible that more positive affect and less depression experienced by the postbypass patients may facilitate their voluntary reduction in food intake.

We also found significant metabolic changes after an intestinal bypass which differ from those after a diet. These included a rise in basal glycerol, a fall in basal insulin, a smaller rise in glucose and insulin after a standard breakfast, and a larger rise in enteroglucagon and pancreatic polypeptide. Dieting alone had no effect on any of these variables. The basal values for these measurements are shown in Table 3.

Glycerol fell slightly after dieting and rose significantly after bypass. Changes in glycerol reflect changes in lipolysis indicating that mobilization of free fatty acids is increased after bypass. This rise in glycerol may

serve as a signal for "satiety." Wirtschafter and Davis recently reported that injecting glycerol into rats lowers food intake and weight gain.[54] The glycerol released from adipocytes is not reutilized by fat cells but is metabolized by muscle and liver. The rate of glycerol release is controlled by insulin concentrations and the size of adipocytes. A fall in insulin is associated with enhanced glycerol. It is thus likely that the enhanced glycerol concentrations are in part related to the fall in insulin concentrations.

The changes in human pancreatic polypeptide are particularly interesting. This peptide contains 36 amino acids and is secreted in response to meals, but not after intravenous glucose, amino acids, or lipids.[1] Moreover, pancreatic polypeptide is depleted from the pancreas in some forms of experimental obesity.[36] Malaisse-Lagae, Carpentier, Patel, and Malaisse recently found that food intake and body weight of obese (ob/ob) mice were reduced after injections of bovine pancreatic polypeptide, and proposed that this peptide might be a factor in regulating food intake and satiety.[37] More recently, Gates and Lazarus have reported that injections of bovine and avian pancreatic polypeptide in New Zealand obese (NZO) mice reduced the hyperglycemia and hyperinsulinemia of these animals as well as normalizing the rate of weight gain.[30] Our data showing that human pancreatic polypeptide rises within 15 minutes after an oral meal, and that there are enhanced and prolonged elevations of this peptide after bypass, make it a possible hormonal candidate for a satiety factor.

Enteroglucagon (gut GLI) was significantly increased in response to the standard breakfast after intestinal bypass (see Fig. 6 and Table 3). However, enteroglucagon was unchanged after dietary weight loss, suggesting that the changes after bypass were not a consequence of weight loss per se. Pancreatic glucagon, on the other hand, was unaltered by either dieting or by intestinal bypass.[17] Recent experimental data and older clinical data have suggested a potential role for glucagon in the control of satiety. Injections of glucagon into normal human subjects significantly reduced food intake.[49] Infusions of purified pancreatic glucagon into the portal vein of experimental animals produced a graded reduction in food intake.[38] Enteroglucagon (gut GLI) in humans is in higher concentrations in the lower part of the intestine.[44] The shortened intestine after an intestinal bypass would thus expose the lower intestine to more food than normal and thus provide a stimulus for release of enteroglucagon. After release, enteroglucagon enters the portal circulation in transit to the liver. Enteroglucagon, like pancreatic glucagon, is glycogenolytic in perfused livers, although less potent.[47] Increased hepatic exposure to enteroglucagon, however, may modulate food intake in man as pancreatic glucagon has been suggested to do in experimental animals.[38]

The changes in insulin are opposite to the other hormones. An improvement in oral glucose tolerance after intestinal bypass has been reported previously[46] and probably reflects reduced absorption of glucose. The lower levels of insulin presumably reflect less need for insulin because of the lower glucose values. The increase in the fasting level of

glycerol after intestinal bypass is also a reflection of the lower insulin value and the subsequent increase in adipose tissue lipolysis. It is conceivable that these alterations in metabolic patterns after surgery may be part of the shift in internal milieu that is responsible for the improved psychosocial responses, increased satiety, and reduced food intake of these patients.

To test the effects of circulating metabolites on hormone secretion and food intake, we have employed the technique described by Thompson and Campbell in which 2-deoxyglucose was used to provoke hunger and thirst in human subjects.[52a] The 2-deoxyglucose was infused into obese patients before and after intestinal bypass, and the effects on food and fluid intake as well as the hormonal systems were measured. We found that the changes in food intake after 2-deoxyglucose were similar both before and after bypass. The stimulation of hormones resulting from cellular glucoprivation with 2-deoxyglucose was also not altered after intestinal bypass, suggesting that the mechanisms involved in modulating feedings after intestinal bypass are not the result of changes which occur in the circulating concentration of metabolites. This negative evidence would argue that it is the alterations in the gastrointestinal tract or hepatic processing of the nutrients or hormones that are involved in reducing the size of meals after bypass.

Summary

The reduction in food intake which follows intestinal bypass is a quantitatively significant portion of the total weight loss. It results from a realignment of eating patterns to normal meal times and a reduction in food intake between meals. There is also a decrease in the size of individual meals. The sweet taste of concentrated solutions of sucrose and glucose is less pleasant. Among the possible mechanisms which might reduce the preference for sweet tasting foods are the losses of zinc and copper which have been demonstrated in patients with an intestinal bypass. After intestinal bypass the intake of two caloric preloads significantly reduced subsequent food intake in relation to the size of the caloric preload. This could not be demonstrated before bypass and might reflect altered nutrient sensitivity in the intestine or altered hormonal responses to the presence of such nutrients.

A comparative study of dieting and intestinal bypass showed that gastric emptying time was unchanged but that insulin and plasma glucose were reduced. There was a corresponding increase in circulating concentrations of enteroglucagon and pancreatic polypeptide. Glycerol concentration also rose. These or other mechanisms might be responsible for the altered food intake after intestinal bypass.

REFERENCES

1. Adrian, T. E., Besterman, H. S., Cooke, T. J. C., et al.: Mechanisms of pancreatic polypeptide release in man. Lancet, *1*:161, 1977.
2. Atkinson, R. L., Dahms, W. T., Bray, G. A., et al.: Parathyroid hormone levels in obesity: Effects of intestinal bypass surgery. Mineral Elec. Metab., *1*:315–320, 1978.
3. Atkinson, R. L., Dahms, W. T., Bray, G. A., et al.: Plasma zinc and copper in obesity and after intestinal bypass surgery. Ann. Intern. Med., *89*:491, 1978.

4. Atkinson, R. L., Dahms, W. T., Lemmi, C., et al.: Gastrin response in obese patients with weight loss from dieting or intestinal bypass. Clin. Res., 25:108A, 1977.
5. Backman, L., and Hallberg, D.: Small intestinal length. An intraoperative study in obesity. Acta Chir. Scand., *140*:57, 1974.
6. Barry, R. E., Barisch, J., Bray, G. A., et al.: Intestinal adaptation after jejunoileal bypass in man. Am. J. Clin. Nutr., *30*:32, 1977.
7. Barry, R. E., Benfield, J. R., Nicell, P., et al.: Colonic pseudo-obstruction: A new complication of jejunoileal bypass. Gut, *16*:903, 1975.
8. Benfield, J. R., Greenway, F. L., Bray, G. A., et al.: Experience with jejunoileal bypass for obesity. Surg. Gynecol. Obstet., *143*:401, 1976.
9. Bray, G. A.,: Intestinal bypass surgery for obese patients—behavioral and metabolic considerations. Psychiatr. Clin. North Am., *1*:673–689, 1978.
10. Bray, G. A.,: Current status of intestinal bypass surgery in the treatment of obesity. Diabetes, *26*:1072, 1977.
11. Bray, G. A.,: The Obese Patient. Philadelphia, W. B. Saunders Co., 1976.
12. Bray, G. A., and Benfield, J. R.: Intestinal bypass for obesity: A summary and perspective. Am. J. Clin. Nutr., *30*:121, 1977.
13. Bray, G. A., and Campfield, L. A.: Metabolic factors in the control of energy stores. Metabolism, *24*:99–117, 1975.
14. Bray, G. A., Faloon, W. W., and Mendeloff, A. I.: Surgical treatment of obesity. Am. Fam. Phys., *15*:111, 1977.
15. Bray, G. A., Barry, R. E., Benfield, J., et al.: Food intake and taste preferences for glucose and sucrose decrease after intestinal bypass surgery. *In* Novin, D., Wyrwicka, W., and Bray, G. A. (eds.): Hunger: Basic Mechanisms and Clinical Implications. New York, Raven Press, 1976, p. 431.
16. Bray, G. A., Barry, R. E., Benfield, J. R., et al.: Intestinal bypass surgery for obesity decreases food intake and taste preferences. Am. J. Clin. Nutr., *29*:779–783, 1976.
17. Bray, G. A., Dahms, W. T., Atkinson, R. L., et al.: Metabolic and behavioral differences between dieting and intestinal bypass. Horm. Metab. Res., in press.
18. Bray, G. A., Zachary, B., Dahms, W. T., et al.: Eating patterns of the massively obese individuals. J. Am. Dietet. Assoc., 72:24, 1978.
19. Bray, G. A., Greenway, F. L., Barry, R. E., et al.: Surgical treatment of obesity: A review of our experience and an analysis of published reports. Int. J. Obesity, *1*:331–367, 1977.
20. Bray, G. A., Passaro, E., Castelnuovo-Tedesco, P., et al.: Intestinal bypass operation as a treatment for obesity. Ann. Intern. Med., *85*:97, 1976.
21. Castelnuovo-Tedesco, P., and Schiebel, D.: Studies of super obesity. II. Psychiatric appraisal of jejunoileal bypass surgery. Am. J. Psychiatry, *133*:26, 1976.
22. Castelnuovo-Tedesco, P., and Schiebel, D.: Studies of superobesity. II. Psychiatric appraisal of surgery for superobesity. Am. J. Psychiatry, *133*:26, 1976.
23. Catalanotto, F. A.: The trace metal zinc and taste. Am. J. Clin. Nutr., *31*:1098, 1978.
24. Chow, A. W., Barry, R. E., Patten, V. et al.: Effect of metronidazole on the intestinal microflora in patients with jejunoileal bypass. Proc. Int. Metronidazole. Montreal, Excerpta Medica, 1978, p. 368.
25. Condon, S. C., Janes, N. J., Wise, L., et al.: Role of caloric intake in weight loss after jejunoileal bypass for obesity. Gastroenterology, *74*:34, 1978.
26. Crisp, A. H., Kalucy, R. S., Pilkington, T. R. E., et al.: Some psychosocial consequences of ileojejunal bypass surgery. Am. J. Clin. Nutr., *30*:109, 1977.
27. Dahms, W. T., Atkinson, R. L., Weitzman, R., et al.: Response of renin, vasopressin and glucoregulatory hormones to intracellular glucopenia. Clin. Res., *127A*, 1978.
28. Dahms, W. T., Atkinson, R. L., Frame, C., et al.: Changes in gut-related hormones in obese patients during weight loss induced by diet or by intestinal bypass. Clin. Res., *26*:109A, 1978.
29. Garner, D. M., Garfinkel, P. E., and Moldofsky, H.: Perceptual experiences in anorexia nervosa and obesity. Canad. Psychiatr. Assoc. J., *23*:249, 1978.
30. Gates, R. J., and Lazarus, N. R.: The ability of pancreatic polypeptide (APP and BPP) to return to normal the hyperglycemia, hyperinsulinemia and weight gain of New Zealand obese mice. Horm. Res., *8*:189, 1977.
31. Glucksman, M. L., and Hirsch, J.: The response of obese patients to weight reduction. III. The perception of body size. Psychosom. Med., *31*:1–7, 1969.
32. Glucksman, M. L., Hirsch, J., McCully, R. S., et al.: The response of obese patients to weight reduction. II. A quantitative evaluation of behavior. Psychosom. Med., *31*:359–373, 1968.
33. Grinker, J., Glucksman, M., Hirsch, J., et al.: Time perception as a function of weight reduction: A differentiation based on age at onset of obesity. Psychosom. Med., *35*:104–111, 1973.
34. Guzman, I. J., Varco, R. L., and Buchwald, H.: Factors determining weight loss after jejunoileal bypass for obesity. J. Surg. Res., *18*:399, 1975.

35. Janowitz, H. D., and Grossman, M. I.: Some factors affecting food intake of normal dogs and dogs with oesophagostomy and gastric fistulas. Am. J. Physiol., *159*:143, 1949.
36. Larsson, L. I., Boder, B. G., and Shaw, W. N.: Changes in islets of Langerhans in obese Zucker rat. Lab. Invest., *36*:593, 1977.
37. Malaisse-Lagae, F., Carpentier, J.-L., Patel, Y. C., et al.: Pancreatic polypeptide: A possible role in the regulation of food intake in the mouse. Experimentia, *33*:915–917, 1977.
38. Martin, J. R., and Novin, D.: Decreased feeding in rats following hepatic-portal infusion of glucagon. Physiol. Behav., *19*:461, 1977.
39. McLean, L. D.: Intestinal bypass operations for obesity: A review. Canad. J. Surg., *19*:387, 1976.
40. Mills, M. J., and Stunkard, A. J.: Behavioral changes following surgery for obesity. Am. J. Psychiatry, *133*:527, 1976.
41. Moberg, S., and Carlberger, G.: Gastric emptying and bile acid concentration in the duodenum after bypass operation of the small intestine because of obesity. Scand. J. Gastroenterol., *11*:151, 1976.
42. Payne, J. H., DeWind, L. T., Schwab, C. E., et al.: Surgical treatment of morbid obesity. Sixteen years of experience. Arch. Surg., *106*:432, 1973.
43. Pilkington, T. R. E., Gazet, J. C., Lang, L., et al.: Explanations for weight loss after ileojejunal bypass. Br. Med. J., *1*:1504, 1976.
44. Polak, J. M., Bloom, S. R., Buchan, A., et al.: Comparative distribution of VIP and EG in man. Gastroenterology, *72*:A-11/821, 1977.
45. Rodin, J., Moskowitz, H. R., and Bray, G. A.: Relationship between obesity and weight loss and taste responsiveness. Physiol Behav., *17*:591, 1976.
46. Sandstead, H. H.: Jejunoileal shunt in morbid obesity. *In* Bray, G. A. (ed.): Obesity in Perspective. Fogarty Int. Ctr. Series on Preventive Med., Vol. 2, Pt. 2. Washington, D.C., U.S. Government Printing Office, 1976, pp. 459–471.
47. Sasaki, H., Ruvalcava, B., Baetens, D., et al.: Identification of glucagon in the gastrointestinal tract. J. Clin. Invest., *56*:135, 1975.
48. Schiebel, D., and Castelnuovo-Tedesco, P.: Studies of superobesity. III. Body image changes after jejuno-ileal bypass surgery. Int. J. Psychiatr. Med., *8*:117, 1977–1978.
49. Schulman, J. L., Carleton, J. L., Whitney, E., et al.: Effect of glucagon on food intake and body weight in man. J. Appl. Physiol., *11*:419, 1957.
50. Sclafani, A., Koopmans, H. S., Vasselli, J. R., et al.: Effects of intestinal bypass on appetite, food intake, and body weight in obese and lean rats. Am. J. Physiol., *234*:E289, 1978.
51. Scott, H. W., Jr., Law, D. H., IV, Sandstead, H. H., et al.: Jejunoileal shunt in surgical treatment of morbid obesity. Ann. Surg., *171*:770, 1970.
52. Smith, G. P., and Gibbs, J.: Cholecystokinin and satiety: Theoretic and therapeutic implications. *In* Novin, D., Wyrwicka, W., and Bray, G. A. (eds.): Hunger: Basic Mechanisms and Clinical Implications. New York, Raven Press, 1976, p. 349.
52a. Thompson, D. T., and Campbell, R. G.: Hunger in humans induced by 2 deoxy-d-glucose: Glucoprivic control of taste preference and food intake. Science, *198*:1065, 1077.
53. Weismann, R. E.: Surgical palliation of massive and severe obesity. Am. J. Surg., *125*:437, 1973.
54. Wirtschafter, D., and Davis, J. D.: Body weight: Reduction by long-term glycerol treatment. Science, *198*:1271, 1977.

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Jejunoileal Bypass for Morbid Obesity

A Bibliographic Study and a Randomized Clinical Trial

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For no less than 20 years, jejunoileal bypass operations have been performed more frequently as a treatment of morbid obesity. A vast amount of literature has appeared on the subject, and current publications are following still faster upon one another. In spite of this, professional opinion as to the advisability of this type of surgery is more divided than ever. Indeed, there are signs that jejunoileal bypass may be discarded in the future and replaced by other operations. Before this happens, it is important that the fairest possible judgment be made about it. For this purpose, I shall try to answer the following questions:

Is jejunoileal bypass good obesity therapy? To decide this issue, one must answer a second question:

What criteria should be met by studies that purport to decide whether obesity therapy, in this case jejunoileal bypass, is good or bad?

Are these criteria met by the abundant literature on jejunoileal bypass? In other words, what can be learned from a bibliographic study?

Are these criteria met by the protocol of the Danish Obesity Project, which was designed with such great expectations? In other words, what can be learned from a randomized clinical trial?

I shall begin by briefly describing the two tools, a bibliographic study and a randomized clinical trial, which I shall apply to answering the last two questions.

Design and Scope of the Bibliographic Study

In collaboration with Erik Juhl and Teis Andersen, a comprehensive survey was made of all publications recorded in the Index Medicus from 1963 to 1977 (first half), dealing with results of the Payne or Scott operations for obesity.[1] The study was based upon a computerized search (MEDLARS), and the keywords of the search program were chosen to identify

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publications fulfilling the following two conditions: primarily, to deal with obesity in combination with either surgery or therapy; secondarily, to deal with surgery and jejunum, or surgery and ileum, or surgery and small intestine.

This study produced a total of 344 references. All these were found and read, if necessary after translation, and 186 were discarded for the following reasons: surveys with no original data (94), double publications (68), type of operation not relevant (such as jejunocolic bypass) or not stated (12), and surgery on animals (12). This left 158 publications. A re-check based upon Phillips' extensive survey from 1978 showed that we had missed 13 (8 per cent), which we subsequently considered to be acceptable.[10] Thus the total number of usable references was 171 (158 + 13), dealing with 6319 patients.

Figure 1 shows the accumulated number of patients and of references related to the year of publication. In cases in which part of a series was previously reported, only the latest publication was included. The vast majority of material dates from the last five years of the 20 years of experience with this treatment.

The curve in Figure 2 outlines the relationship between the cumulated percentages of references and of patients. Fifty per cent of the articles deal with only 5 per cent of the patients. Conversely, if information is desired about half of the patients, more than 90 per cent of the literature may need to be read. Almost two-thirds of the articles and three-fourths of the patients are of United States origin (Table 1). About half of the patients are operated on with Payne's anastomosis (2994 patients or 47 per cent), one third with Scott's modification (2175 patients or 34 per cent), with the remainder of operations mixed or not stated (1150 patients or 18 per cent).

Design and Scope of the Randomized Clinical Trial

Noninvasive treatment of obesity is notoriously disappointing in achieving and maintaining weight loss. Though effective in this respect, jejunoileal bypass soon proved to entail sizeable mortality and numerous undesirable sequelae, which should be weighed against the risks of persisting extreme obesity, for which there is little statistical documentation.

Table 1. *Bibliographic Study of Jejunoileal Bypass for Obesity: The Most Prominent Publishing Countries*

	NUMBER OF REFERENCES	NUMBER OF PATIENTS	PER CENT
United States	105	4816	76
Sweden	10	359	6
Great Britain	13	352	6
Denmark	12	254	4
West Germany	3	207	3
Canada	4	148	2
Norway	6	42	1
Poland	5	40	1
Others or not stated	13	101	2
TOTAL	171	6319	101

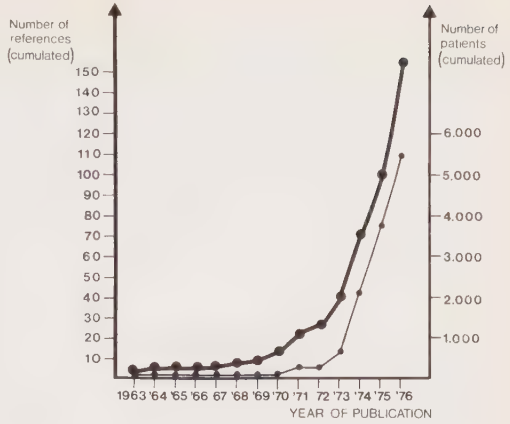

Figure 1. Bibliographic study of jejunoileal bypass for obesity. Year of publication in relation to cumulated number of patients and of references.

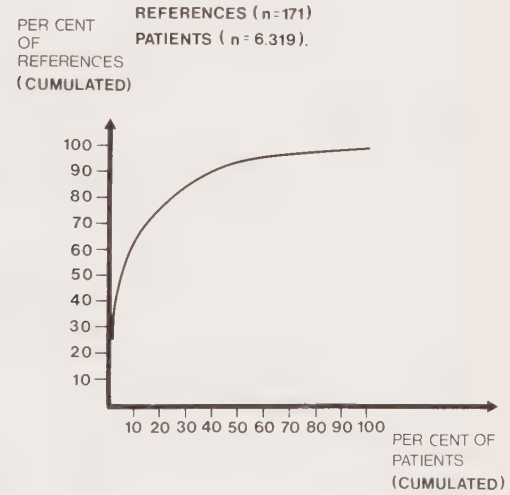

Figure 2. Bibliographic study of jejunoileal bypass for obesity. Relation between number of references and number of patients.

In the absence of a surgical procedure for obesity so effective and at the same time so harmless that it would convince everybody of its efficacy, even in an open trial, the value of any surgical approach has yet to be proved in controlled comparison with either current medical therapy or no treatment at all.

For these reasons, 12 Danish hospitals, medical and surgical, agreed to comply with a common protocol in a randomized trial comprising patients with massive obesity referred between September 1973 and September 1976. The results in the following analysis show the status of the trial in April 1979, after a minimal observation time of 2½ years. The principles of the protocol are outlined in Figure 3, and the general data of the 196 patients available for assessment appear below. For further details the reader is referred to previous publications.[5, 11, 12]

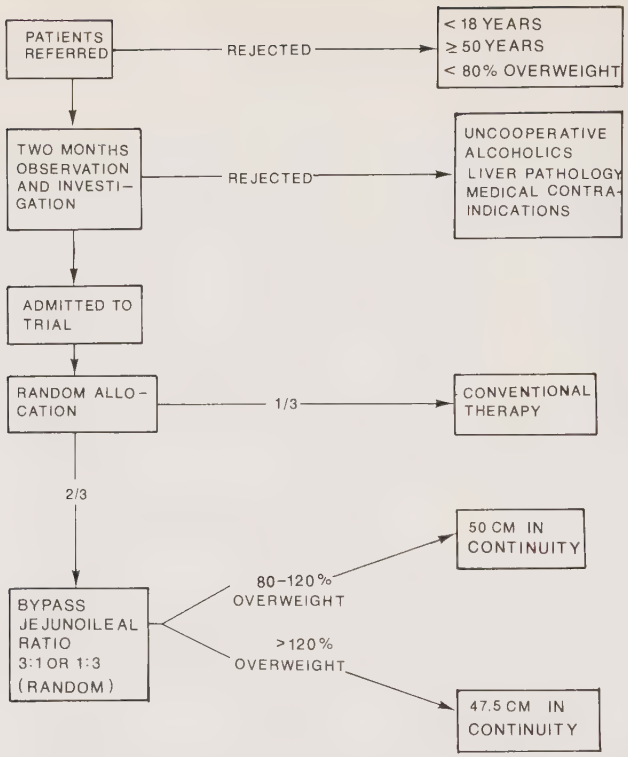

Figure 3. Flow chart for randomized clinical trial of shunt operation for obesity treatments.

Age: 32.2 years (18 to 50 years)
Weight: 125.3 kg (90 to 213 kg)
Height: 166.4 cm (145 to 190 cm)
Males: 16 per cent
Females: 84 per cent
Medical treatment: N = 66
3:1 jejunoileal ratio: N = 64
1:1 jejunoileal ratio: N = 66

WHAT SHOULD BE DEMANDED OF A THERAPEUTIC OBESITY STUDY AND HOW THESE DEMANDS ARE MET BY THE BIBLIOGRAPHIC STUDY AND RANDOMIZED CLINICAL TRIAL

A number of requirements, most of them standard, some ideal and theoretical, some merely obvious and practical, related to scope, design, evaluation, and recommendation should be met whenever obesity therapy, in this case jejunoileal bypass, is adopted and written about. For each item, an attempt is made to match these demands with information distilled from the bibliographic study or the randomized clinical trial, or both.

Definition of Morbid Obesity

Adequate definition of morbid obesity is arrived at by stratification with regard to various types of obesity, such as childhood onset versus adult onset, hyperplastic versus hypertrophic, hyperphagic versus nonhyperphagic, alcoholics versus nonalcoholics, and also sex, ethnic group and socioeconomic status. Stratification is desirable to minimize interpersonal variation, and because the possibility should be anticipated that one or more subgroups will significantly benefit from the operation or be harmed by it.

On most of these points, the bibliographic study is unsatisfactory. Only 34 of the 171 articles specified the overweight criterion, and stratification was virtually nonexistent, if only because many patient groups were too small for the purpose (see Fig. 2). The randomized clinical trial, which with its nearly 200 patients had no such excuse, also neglected this point at the planning stage, and will have to compensate for it in later evaluations, by trying to define, in retrospect, risk groups or probable successful patients.

Description of Patient Sample

Obese target populations should be adequately defined from a description of the patient sample entering the study. The motives for patients being included in or excluded from the sample should be defined, as should the reasons why some patients drop out. If not, valid conclusions cannot be drawn with regard to the target population, and with regard to morbidly obese patients in general.

The bibliographic study satisfies this requirement only to a certain extent. It comes mainly from the United States, with many ethnic groups, and the patients are largely self-selected by dissatisfaction with the obese state, by a desire for surgery, and probably also by their economic status. Very little is known about the morbidly obese person who does not strive to obtain surgery or, for that matter, other treatment. Our randomized clinical trial may fare somewhat better in this respect. The Danish population is ethnically and economically more homogenous, the treatment is not being paid for, and by no means were all of our patients referred to us because they wanted surgery; some had not even heard of it.

Random Allocation

Random allocation to treatment and control groups, the latter receiving either no treatment or some type of medical therapy, is mandatory. The bibliographic study showed that our randomized clinical trial is the only existing trial of this design. This is understandable. In the United States, which dominates the field of obesity surgery, and hence the bibliographic study, the patient's independence and exclusive request for surgery would probably make randomization to a stable control group impossible. However, important studies from the United States have randomized patients to either gastric or jejunoileal bypass,[3, 7] and to either the Payne or Scott operations.[8]

Informed Consent

True informed consent should be obtained; this, in turn, raises the problem of self-selection. The Danish randomized clinical trial was initiated before the Helsinki II declaration of 1975, and although we did explain the nature and likely consequences of surgery to patients, we did not, until recently, after the advent of the said declaration, tell them that their allocation would be decided by the toss of a coin. Without doubt, a strong and unpredictable element of selection will be introduced by the concept of informed consent in future randomized trials. Many patients will fail to understand that the doctor cannot make up his professional mind and that he is in real doubt as to whether a life-changing operation should be performed; such patients may refuse to enter the study. The patients who do understand the doctor's dilemma may prove to be of a special intellectual or emotional type, making the description of the target population illusory.

Prospective Design and Protocol

Naturally, all articles of the bibliographic study attempt some description of obese patients and their motives for resorting to surgery, but as a rule this is done in retrospect and in vague and general terms. The bibliographic study revealed an astonishing paucity of specified positive and negative criteria for eligibility that were respected before surgery was decided upon. Such criteria were defined in only one-fourth of the 171 publications; they are listed in order of frequency in Table 2.

It is reasonable that degree of overweight is taken into consideration, but it is not necessarily the best criterion. Few, if any, very obese persons have not tried conservative treatment, so this criterion is so obvious that it is of little practical importance. The same can be said about minimum duration, as massive obesity is a chronic condition which takes time to be

Table 2. *Bibliographic Study of Jejunoileal Bypass for Obesity: Criteria for Eligibility Decided Upon Before Surgery*

CRITERIA	PER CENT OF 42 REFERENCES WITH CRITERIA SPECIFIED
Degree of overweight	81
Failure of conservative treatment	69
Ability to cooperate	52
Absence of endocrinopathy	40
Minimum duration of obesity	38
Psychiatric evaluation	33
Presence of somatic complications	17
Increased operative risk	17
Maximum age	17
Minimum age	10
Presence of psychosocial handicap	5
Alcoholic liver affliction	5
Absence of alcoholic abuse	5
Others	21

Table 3. *Bibliographic Study of Jejunoileal Bypass for Obesity: Publishing Hospital Departments*

HOSPITAL DEPARTMENT	NUMBER OF REFERENCES	PER CENT
Surgical without medical	82	48
Medical without surgical	22	13
Medical and surgical	34	20
Others or not stated	33	19
TOTAL	171	100

acquired, and as there is little reason to hope that the rare case of recently developed massive obesity will resolve of its own accord. Equally unimportant is hormonal disorder as a proved and curable cause of morbid obesity.

In view of the prominence of these self-evident or theoretical criteria, one may wonder why factors such as age limits, psychosocial maladjustment, alcoholism, and alcoholic liver affliction are at the bottom of the list. Only one-third of the 42 references include a preoperative psychiatric evaluation, and we admit openly that the randomized clinical trial is not among them. Almost half the reports of the bibliographic study are issued from surgical departments with no indication of responsible coauthorship with internists or a psychiatrist, and joint publications from surgical and medical departments make up only 20 per cent (Table 3).

Adequate Follow-Up Evaluation

Frequency of work-up of postoperative and control subjects, and duration of follow-up are other disappointing protocol items from the bibliographic study, in view of the fact that so many patients are known to have been operated on over so many years. For example, with regard to weight loss (Fig. 4) there are only 45 publications (1711 patients) related to

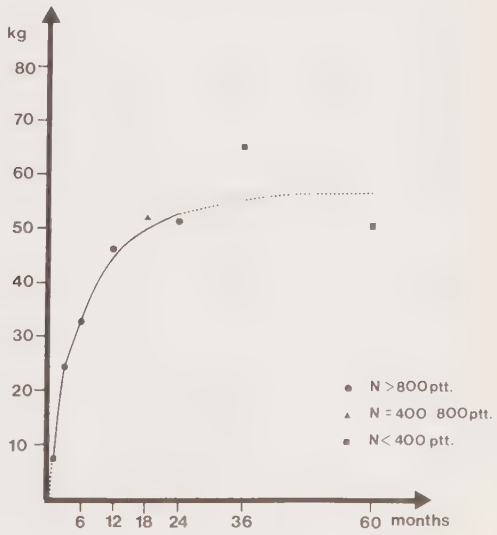

Figure 4. Bibliographic study of jejunoileal bypass for obesity. Postoperative weight loss.

observations after one year, and the five year point is reported by a mere five references (346 patients). Many operated patients in the United States are lost to follow-up at an early stage for reasons of methodology, geography, and economy. We have done somewhat better in tiny and bureaucratic Denmark. Still, in the control group of the randomized clinical trial, 14 of 66 patients were lost to follow-up after a median period of nine months, as were two of the 130 operated patients in the second year after surgery.

According to the protocol of the randomized clinical trial, participating departments are now free to operate on control patients, and some of our surgeons are in the process of doing this. Other departments, such as my own, have so far been able to retain the unoperated patients in the study under conservative treatment and to avoid their having surgery elsewhere. We realize, however, that this attitude cannot be prolonged indefinitely if the new treatments deliver what they promise.

Weight Loss Criteria

Proper criteria for therapeutic efficacy, in the limited sense, are compilations of pounds lost. As indicated before, many bibliographic studies either do not mention weight loss, or they fail to relate it to time of follow-up. Figure 4 shows that an average of 50 kg is lost after two years in the bibliographic study. The randomized clinical trial did not reveal anything unexpected: the operated patients lost much more weight than the controls ($P < 0.001$). However, it is worth noting that significant amounts of weight were also lost in the conservatively treated group ($P < 0.01$); 24 months after randomization the median weight loss was 5.0 kg (range, 11.9 to 40.4 kg). The corresponding figure in the operated group was 42.9 kg (range, 20.5 to 108.5 kg). Beyond 24 months, we have seen only minor alterations in weight, a few being moderate late weight gains. Still, the majority of the operated patients in the randomized clinical trial are still overweight. While 54 per cent are less than 30 per cent above normal, only 11 per cent have attained normal weight. The 3:1 and 1:3 jejunoileal techniques were equally effective in producing weight loss.

Quality of Life Criteria

Therapeutic efficacy in the wider sense of an improved quality of life, taking into account the undesirable postoperative occurrences (discussed later under Untoward Postoperative Sequelae), is essential in treatment analysis. How bad is the quality of life in respect to increased morbidity and psychosocial maladjustment, in the conservatively treated (and therefore mostly persisting) condition of morbid obesity? Is quality of life any better after jejunoileal bypass? Is it at all possible to compare the problems of obese patients with the operated patients' reactions to the tribulations of the malabsorption syndrome, which in 1973 was the alternative to remaining fat?

Most studies of the bibliographic study do not analyze postoperative quality of life in any depth, and those that do make a retrospective comparison of situations before and after surgery, with patients serving as their own controls. On the whole, the reports are favorable.[6, 9, 13] After

weight loss psychosocial amelioration is reported, primarily as less self-dislike, insecurity, and sense of failure. Also noted are improvements in working capacity, leisure time activity, and interpersonal relationships, including sexual life.

In the randomized clinical trial, a cross-sectional evaluation of quality of life was attempted in 1977. A questionnaire with a total of 177 questions about social circumstances and somatic and psychological symptoms was sent to all patients with a post-randomization time of at least 15 months, that is, 110 operated patients and 52 controls. Usable answers were obtained from 94 per cent. A comparison between operated and unoperated patients with regard to some characteristic somatic complaints is provided in Table 4. As might be expected, gastrointestinal discomfort dominates in the operated group, but we are reminded that it is also frequent in obesity. Shortness of breath and cardiac discomfort were more pronounced among the controls, as were various musculoskeletal complaints. A characteristic difference is seen in adaptability to heat and cold. The patients' rating of their psychological adaptation to the operated or unoperated (obese) state points to an improvement after bypass (Table 5). The same is true of the social factors (Table 6). The frequency of social contacts outside the family, expressed as the monthly number of visits from or to friends, was twice as high in the operated as in the unoperated group. Most of the former did not regret having undergone the operation and would have chosen surgery again. It must, however, be admitted that no differences were found between the two groups regarding the important factors of employment, absence from work, disability pension, marital status, and housing or economic status.

Of course, there are several criticisms of the randomized clinical trial quality of life study. One is that the control patients received different

Table 4. *Statistically Significant Differences in Somatic Symptoms in Operated and Nonoperated Patients in the Randomized Clinical Trial*

SOMATIC SYMPTOM	MEDICAL GROUP 52 PATIENTS (PER CENT)	SURGICAL GROUP 110 PATIENTS (PER CENT)
Dyspnea on slight exertion	42	14‡
Precordial pain	21	7*
Heartburn	38	14‡
Abdominal pain or discomfort	54	87‡
Flatulence	40	93‡
Anal complaints	17	40†
Low back pain	63	41†
Pain in hips, knees, or ankles	67	22‡
Excessive sweating	54	15‡
Intolerance to heat	69	22‡
Intolerance to cold	6	39‡
Dermal irritation or rashes	77	16‡

*$0.05 > P > 0.01$, χ^2 test, df = 1.
†$0.01 > P > 0.001$, χ^2 test, df = 1.
‡$0.001 > P > 0.0001$, χ^2 test, df = 1.

Table 5. *Statistically Significant Differences in Psychological Complaints in Operated and Nonoperated Patients in the Randomized Clinical Trial*

PSYCHOLOGICAL COMPLAINT	MEDICAL GROUP 54 PATIENTS (PER CENT)	SURGICAL GROUP 110 PATIENTS (PER CENT)
Excessive fatigue	69	41†
Periodic depression	62	36*
Periodic irritability	71	41†
Feelings of insecurity	65	40*
Feelings of inferiority or insufficiency	65	37†
Feelings of isolation	35	11†
Feelings of loneliness	35	14*
Feelings of being despised	69	21†

*$0.01 > P > 0.001$, χ^2 test, df = 1.
†$0.001 > P > 0.0001$, χ^2 test, df = 1.

Table 6. *Statistically Significant Differences in Social Factors in Operated and Nonoperated Patients in the Randomized Clinical Trial*

SOCIAL FACTOR	MEDICAL GROUP 52 PATIENTS (PER CENT)	SURGICAL GROUP 110 PATIENTS (PER CENT)
Exercise daily	35	55*
Participates in organized sports	12	26*
"Normal" sexual life	52	78†
Can wear ready made clothes	46	96†
Socially satisfied	52	76†
Sexually satisfied	48	82†

*$0.05 > P > 0.01$, χ^2 test, df = 1.
†$0.001 > P > 0.0001$, χ^2 test, df = 1.

medical treatments carried out with greatly varying dedication. The control patients in the participating surgical departments were the ones who hoped most for bypass eligibility, while at the same time they were given the least effective conservative help. Naturally, such persons will stress their dissatisfaction with their continuing state of obesity.

The design of our study, though formally attractive, and comparing randomized groups, sometimes defeated its own purpose. By the operation, one group embarks upon a course so different from the other that they cannot be meaningfully compared psychologically or somatically. It is futile to speculate which is worst: to have gas pains or aching knees. Still, some degree of satisfaction with surgery prevails, in spite of the often impressive side effects endured by the patients allocated to jejunoileal bypass. This has left me with the impression that after surgery, the patient's acceptance is often greater than the doctor's acceptance (see conclusion).

Criteria for Undesirable Occurrences

Benefits must be weighed against all undesired occurrences, ranging from minor side effects to lethal outcome. Death after jejunoileal bypass was reported in 2.8 per cent of the bibliographic studies (Table 8). This is a minimal figure, because nearly half of the publications do not mention mortality rate. Only 21 per cent of the 179 fatal cases occurred within the first postoperative month (Table 7), and afterward patients are by no means safe, as a minimum of 90 patients have died at a later time. In the randomized clinical trial, there have so far been no deaths in the operated group (95 per cent confidence limits of fatality rate; 0.0 to 2.7 per cent). One patient in the control group died from a succession of unusual complications resulting from a liver biopsy. Autopsy showed that liver cirrhosis had developed after the pre-randomization biopsy.

Thus, in the randomized clinical trial, sizes of groups and observation times are too small for us to make a conclusion regarding mortality. With respect to the literature at large, one might speculate whether at present a new drug carrying a mortality of at least 3 per cent would pass the censure of the United States and Scandinavian health authorities.

Untoward Postoperative Sequelae

Frequency and gravity of all complications should be registered and included in the evaluation. In the majority of the bibliographic study publications, many of the recognized postoperative sequelae are either not mentioned, or they deal with patient groups so small that frequencies cannot be calculated. Many are case histories describing a new complication in one or a few patients. Other authors publish when they observe the first serious or fatal complication in a newly started series (these facts help to explain Figure 2).

In the bibliographic study, we have taken the position that reasonably reliable frequencies of complications can be obtained only from articles with more than 50 patients, which explicitly mention the presence or absence of the complication and quantify its occurrence. From these selected reports, the complications are ranked by frequency in Table 8. The numbers of references involved are also stated in the table, because they tell us something about the attention that the authors gave to the complication in question. An example is liver injury, by which is meant clinical illness, and not merely steatosis or biochemical abnormality.

Table 7. *Bibliographic Study of Jejunoileal Bypass for Obesity: Postoperative Mortality*

TIME AFTER OPERATION	NUMBER OF PATIENTS	PER CENT
Less than one week	16	9
One week to one month	21	12
One month to six months	42	23
More than six months	48*	27
Not stated	52*	29
TOTAL	179	100

*One suicide included.

Table 8. *Bibliographic Study of Jejunoileal Bypass for Obesity: Complications and Undesirable Effects*

COMPLICATION	ALL 171 REPORTS		SELECTED REPORTS (≥ 50 PATIENTS)		
	Number of Patients With the Complication	Per Cent of All Patients	Number of Patients With the Complication	Number of Patients With Information About the Presence or Absence of the Complication	Per Cent
Wound complications	315	5.0	231	1.228	18.8
Hypokalemia	299	4.7	211	1.218	17.3
Severe diarrhea	307	4.9	90	611	14.7
Hypomagnesemia	203	3.2	99	688	14.4
Hypocalcemia	221	3.5	150	1.083	13.9
Hemorrhoidectomy	55	0.9	35	252	13.9
Pneumatosis intestinalis	34	0.5	28	272	10.3
Arthritis syndrome	73	1.2	56	683	8.2
Kidney stones	154	2.4	127	1.614	7.9
Gallstones	53	0.8	43	704	6.1
Psychologic complications	26	0.4	21	354	5.9
Intestinal obstruction	14	0.2	14	240	5.8
Megacolon	20	0.3	10	227	4.4
LED-like syndrome	2	0.0	2	52	3.8
Liver injury	183	2.9	83	2.567	3.2
Peptic ulcer	9	0.1	6	278	2.2
Invagination	20	0.3	14	669	2.1
Severe flatulence	18	0.3	2	157	1.3
Leg thrombosis	15	0.2	9	702	1.3
Pulmonary embolism	43	0.7	30	2.630	1.1
Tuberculosis	6	0.1	1	103	1.0
Anastomotic leak	12	0.2	11	1.165	0.9
Suicide	2	0.0	2	503	0.4
Hypocobalaminemia	28	0.4	0	650	0
Excessive weight loss	13	0.2	3	663	0.5
Inadequate weight loss	137	2.2	95	1.079	8.8
Reoperation:					
Shunt shortening	63	1.0	38	963	3.9
Shunt lengthening	13	0.2	8	157	5.1
Reanastomosing	60	0.9	27	1.502	1.8
Death	179	2.8	137	3.151	4.3

The rate of complications in operated patients in the randomized clinical trial has been acceptable by bibliographic study standards, and need not be mentioned in detail, except for the fact that renal stones are seldom a problem. The reason for this seems to be that we routinely give large doses of calcium powder to prevent diarrhea.

Statement of the Author's Attitude

Whenever feasible, the author's attitude should be stated, and its rationale revealed. Two-thirds of the references neither recommend nor deprecate jejunoileal bypass (Table 9). With a few exceptions, the remaining third either express uncertainty toward its advisability (12 references), or are positive with various, vaguely expressed reservations (40 references).

These two subgroups, providing information on the author's assessment, were examined and compared with regard to the following parameters: nation of origin, year of publication, type of department, number of patients, observation time, weight loss achieved, type of operation, and number of deaths. At the 5 per cent confidence level no significant differences were found. Oddly enough, at the 10 per cent confidence level there were significantly more fatal cases in the reports with a positive attitude. Equally surprising, at the same level of significance, the positive reports were published more recently than the negative and uncertain ones. All too often, a conclusion is made along this line: "In carefully selected patients and under competent control jejunoileal bypass has a place in the treatment of massive obesity."

I hasten to admit that we, the fathers of the randomized clinical trial, are no better in this respect. In spite of an elaborate protocol, we have been unable to reach consensus on the interpretation of our results, and consequently on the future advisability of jejunoileal bypass. On the whole, the participating internists are more reserved than the surgeons. Speaking only for myself, and not as an official representative of the Danish Obesity Project, I venture the following concluding remarks.

Table 9. *Bibliographic Study of Jejunoileal Bypass for Obesity: Authors' General Attitudes Toward the Operation*

	NUMBER OF REFERENCES	PER CENT
Strongly negative	1	1
Negative	1	1
Uncertain	12	7
Positive with reservation	36	21
Strongly positive	4	2
None	117	68
Total	171	100

CONCLUSION

Regardless of its spectacular effect on body weight, jejunoileal bypass remains a major physical intervention, carrying with it a sizeable mortality and a long list of side effects, both of which are of questionable professional acceptability, even in the absence of any effective therapeutic alternative. In my view, the quality of life studies merely prove the important point that reduced weight and restored psychosocial and cosmetic acceptability are of overriding importance for most of these patients. Patient acceptance of jejunoileal bypass is on the whole high because the operated patient copes better psychologically with the postoperative side effects than does the unoperated patient with the continued burden of obesity. The original rationale, that weight loss after jejunoileal bypass is due to fecal loss of calories, and that any restraint in food intake is caused by fear of colic and increased diarrhea, is too simplistic. Evidence is accumulating to prove that the main reason for weight loss is an improvement in quantitative and qualitative food intake.[2, 4] Also, weight loss and dietary accommodation after both small bowel and gastric surgery are achieved with less anxiety, depression, irritability, and preoccupation with food than is a comparable weight reduction through adherence to a conventional diet.[11] There is now reason to hope that these goals can be approached by less hazardous measures than jejunoileal bypass; gastric bypass, gastroplasty, jaw wiring, vagotomy, and protein supplemented modified fasting are alternatives of promise. This promise may also be fulfilled when cost-benefit considerations of time, money, and resources generally are taken into account. Therefore, it is my feeling that we may soon have witnessed the last jejunoileal bypass operation for morbid obesity.

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Steering committee: B. Andersen and H. Baden, Herlev Hospital, University of Copenhagen, E. Juhl and F. Quaade, Hvidovre Hospital, University of Copenhagen.

Participants: O. Backer (Bispebjerg Hospital), E. Gudmand-Høyer (Gentofte Hospital), B. Andersen and H. Baden (Herlev Hospital, University of Copenhagen), P. Martiny (Holstebro Hospital), E. Juhl, F. Quaade and K. H. Stokholm (Hvidovre Hospital, University of Copenhagen), O. Noring (Nykøbing Falster Hospital), O. Iversen and S. Madsen (Næstved Hospital), C. M. Madsen and E. M. Mogensen (Odense Hospital, University of Odense), K. Gotlieb Jensen (Ribe Hospital), A. Marckmann (Sønderborg Hospital), K. Emmertsen, K. E. Petersen and U. Starup (Vejle Hospital), D. Andersen, L. Mosekilde and N. Schwartz Sørensen (Århus County Hospital, University of Århus).

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REFERENCES

1. Andersen, T., Juhl, E., and Quaade, F.: Jejunoileal bypass for obesity—What can we learn from the literature? Am. J. Clin. Nutr., in press.
2. Bray, G. A., Barry, R. E., Benfield, J. R., et al.: Intestinal bypass surgery for obesity decreases food intake and taste preferences. Am. J. Clin. Nutr., 29:779, 1976.
3. Buckwalter, J. A.: A prospective comparison of the jejunoileal and gastric bypass operations for morbid obesity. World J. Surg., *1*:757, 1977.
4. Condon, S. C., Janes, N. J., Wise, L., et al.: Role of caloric intake in the weight loss after jejunoileal bypass for obesity. Gastroenterology, 74:34, 1978.
5. Danish Obesity Project: Randomised trial of jejunoileal bypass versus medical treatment in morbid obesity. Lancet, in press.
6. Danø, P., and Hahn-Pedersen, J.: Improvement in quality of life following jejunoileal bypass surgery for obesity. Scand. J. Gastroenterol., *12*:769, 1977.
7. Griffen, W. O., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. Ann. Surg., *186*:500, 1977.
8. Jewell, W. R., Hermreck, A. S., and Hardin, C. A.: Complications of jejunoileal bypass for morbid obesity. Arch. Surg., *110*:1039, 1975.
9. Mills, M. J., and Stunkard, A. J.: Behavioral changes following surgery for obesity. Am. J. Psychiatry, *133*:527, 1976.
10. Philips, B. R.: Small intestine bypass for the treatment of morbid obesity. Surg. Gynecol. Obstet., *146*:455, 1978.
11. Quaade, F., and Danish Obesity Project: Studies of operated and non-operated obese patients. An interim report. Am. J. Clin. Nutr., 30:16, 1977.
12. Quaade, F., and Danish Obesity Project: Intestinal bypass for severe obesity. A randomized trial. Recent advances in obesity research II. London, Newmann Publishing, Ltd., 1978.
13. Solow, C., Silberfarb, P. M., and Swift, K.: Psychosocial effects of intestinal bypass surgery for severe obesity. New Engl. J. Med., *290*:300, 1974.
14. Halmi, K. A., Stunkard, A. J., and Mason, E. E.: Emotional responses to weight reduction by three methods: Gastric bypass, jejunoileal bypass, diet. Am. J. Clin. Nutr., in press.

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Oxalate Urolithiasis Following Jejunoileal Bypass

Mechanism and Management

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The proclivity of the patient who has undergone jejunoileal bypass to form renal stones represents one of the more frequent complications of intestinal bypass surgery.[24, 30] In 1970, Hofmann and associates reported two patients with ileal resection and associated hyperoxaluria.[16] Three years later Dickstein and Frame found two patients with symptomatic calcium oxalate stones among 11 patients who had undergone intestinal bypass.[11] Since then the prevalence of post-bypass stone disease has been recorded at the 11 per cent level by many series, encompassing over 2000 jejunoileal bypass patients (Table 1). It must be noted, however, that this 11 per cent figure does not include patients with asymptomatic stone disease, since intravenous pyelography is rarely a part of the routine postoperative protocol. O'Leary obtained abdominal roentgenograms as part of his postoperative regimen and found the prevalence of urolithiasis to be 23 per cent.[21]

Of significance among the stone-forming bypass population is that the prevalence of renal calculi among male patients is 20 per cent, as opposed to only 7 per cent in female patients.[8, 9] An unexplained higher prevalence of urolithiasis in the general male population has been documented as well. Also of note is the higher risk for stone formation among jejunoileal bypass patients with a prior history of urolithiasis,[11] implying that such a history is a relative contraindication to intestinal bypass surgery.

Most patients who have stone formation following jejunoileal bypass have a single attack of symptomatic stone disease within the first two years of surgery. Most of the stones are small enough that they pass spontaneously. However, approximately one-fifth of patients with stone disease will require hospital admission and subsequent pyelolithotomy or

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Table 1. *Summary of Previous Studies on Urolithiasis Following Jejunoileal Bypass*

AUTHORS	NO. OF PATIENTS STUDIED	PATIENTS WITH STONES (PER CENT)	TIME FROM OPERATION TO SYMPTOMATIC STONE	PATIENTS WITH MORE THAN ONE STONE (PER CENT)	COMPOSITION	STONE-RELATED OPEN OPERATION (PER CENT)
Payne[22]	230	14	–	–	Calcium oxalate	–
Salmon[25]	150	2	–	–	1 pt.—Cystine. Remainder—Calcium oxalate	–
Fikri[10]	52	10	9 mos. (5–13 mos.)	80 (4 patients)	Calcium oxalate	80
Dickstein[8]	11	18	17 mos. (24 d.–6 yrs.)	100 (2 patients)	Calcium oxalate	0
Gregory[14]	380	16	Per cent of total stones: 1 yr. postop.—57 per cent 2 yrs. postop.—18 per cent 3 yrs. postop.—17 per cent 4 yrs. postop.— 7 per cent	41	2 pts–NH_4 urate. Remainder—Calcium oxalate	12
O'Leary*[21]	31	23	11 mos. (1.5–33 mos.)	–	Calcium oxalate	–
Thomas[31]	100	14	–	24 stones in 14 patients	Calcium oxalate	21
Jewell[18]	52	6	–	–	Calcium oxalate	–
Clayman[6]	365	9	22 mos. (3–44 mos.)	33	Calcium oxalate	21
Halverson[15]	101	8	16 ± 11 mos.	–	Calcium oxalate	–
Gourlay[13]	261	2.5	–	–	2 pts. Calcium oxalate	28
Telmos[30]	169	21	–	–	Calcium phosphate	–
					Calcium oxalate	–
Mersheimer[19]	51	4	–	–	–	0
Scott[26]	200	14.5	–	–	–	–
Total or Mean	2153	11		42		19

*Three stones noted on routine follow-up roentgenograms of abdomen in asymptomatic patients.

ureterolithotomy. In some, recurrent stone formation will necessitate reversal of the bypass procedure. More ominous than the stone formation is the rare occurrence of renal failure associated with oxalosis and nephrocalcinosis.[12, 20] The potential seriousness of these renal complications has been underscored by DeWind and Payne who noted that 20 per cent of all bypass-related deaths were secondary to associated renal problems.[7, 22]

MECHANISM FOR ACQUIRED HYPEROXALURIA

Oxalic acid (HOOC-COOH) is derived from either hepatic glycine metabolism or enteric absorption of foodstuffs containing oxalate (rhubarb, cocoa, tea, leafy green vegetables). Under normal circumstances, the liver is responsible for 90 per cent of the oxalate excreted in the urine. Both glyoxylic acid derived from glycine degradation and ascorbic acid are metabolized to oxalic acid. Alternatively oxalate may be ingested and passively absorbed in the colon.[17] However, only 5 to 15 per cent of the ingested oxalate load (approximately 200 mg per day) is normally absorbed.[14] The bulk of ingested oxalate is complexed with enteric calcium to form an insoluble, nonabsorbable salt which is eliminated as fecal waste. Thus, the normal urinary oxalate concentration of less than 40 mg per 24 hours is derived only in small part from direct colonic absorption of ingested oxalate, while the bulk is secondary to hepatic metabolism of glycine (Fig. 1).

Hyperoxaluria in the jejunoileal bypass patient could be secondary to alterations in either the hepatic or the enteric oxalate pathway. The disruption of the enterohepatic bile salt cycle and the ensuing postbypass changes in liver function were the earliest explanations for the hyperoxaluric state.[16] To study this possibility, Chadwick and others administered known hepatic precursors of oxalate: oral ^{14}C-labelled glycine

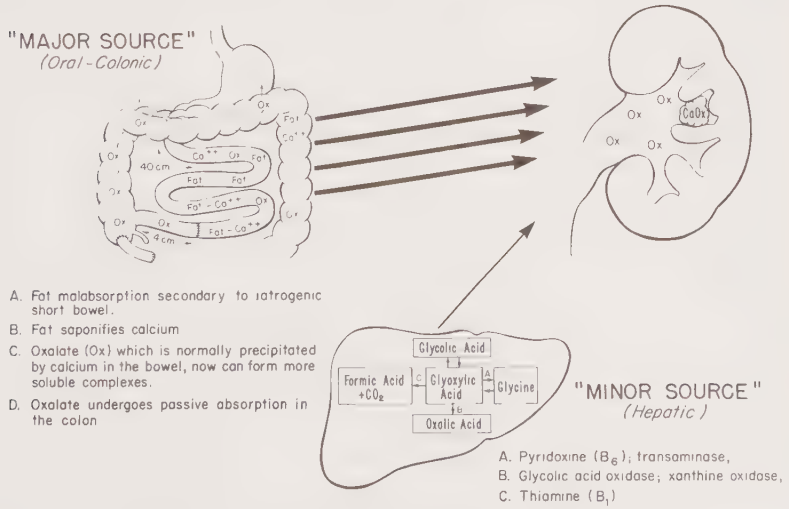

Figure 1. Sources of oxalate in jejunoileal bypass patients.

and parenteral glyoxylate. Their results failed to corroborate a hepatic etiology for postoperative hyperoxaluria.[4, 5]

To examine the possibility of hyperoxaluria on the basis of excessive intestinal absorption, investigators gave jejunoileal bypass patients oral loads of pure, as well as radioactively labelled, oxalate. In studies independently performed by Chadwick, Earnest, and Gregory, it was noted that while the preoperative obese patient absorbed approximately 5 to 15 per cent of an oral oxalate load, the postoperative patient absorbed 50 per cent or more.[4, 9, 14] These findings are in agreement with similar studies on renal stone formation in patients with inflammatory small bowel disease. Specifically, in patients with an intact colon, hyperoxaluria can result when more than 100 cm of ileum are resected. In contrast, patients with an ileostomy do not have an increased tendency for hyperoxaluria.[9]

Among jejunoileal bypass patients as well as among patients with inflammatory small bowel disease, rapid transit time and malabsorption result in steatorrhea. The excess enteric fat binds to intraluminal calcium to form intestinal soaps. This decrease in free enteric calcium precludes precipitation and fecal elimination of oxalate as the insoluble salt (calcium oxalate). Consequently, oxalate remains in a more soluble form and, upon reaching the colon, it is passively absorbed. The enteric theory for hyperoxaluria in patients with intestinal bypass is further supported by studies showing an increase in urinary oxalate following rectal administration of ^{14}C-oxalate and the effective decrease in urinary oxalate in jejunoileal bypass patients on an oxalate-free diet.[2, 14] Accordingly, in the jejunoileal bypass patient with an intact colon and a loss of over 350 cm of ileum, the ensuing three-fold increase in urinary oxalate excretion (100 to 120 mg per 24 hours) is understandable.[17, 31]

MANAGEMENT OF OXALATE UROLITHIASIS

The transformation from the hyperoxaluric state to symptomatic stone disease is less well understood. The formation of renal oxalate calculi is dependent upon two variables: the urinary concentration of stone-forming substances (calcium and oxalate) and the urinary concentration of stone-inhibiting substances (magnesium and pyrophosphate). In the patient with a jejunoileal bypass, the interaction of these two factors likely accounts for the presence of symptomatic stones in only one-tenth of this patient population despite hyperoxaluria in almost 90 per cent. As such, prophylactic therapy for oxalate stone formation in jejunoileal bypass patients is directed toward either decreasing those components necessary for calculus formation or increasing those substances in the urine known to inhibit oxalate crystallization.

In the jejunoileal bypass patient, urinary calcium is most often in the normal or low normal range. Furthermore, the contribution of urinary calcium concentration to oxalate stone formation is not as important as the urinary oxalate concentration. In fact, Robertson has shown that whereas a 70 per cent increase in urinary calcium levels failed to increase calcium oxalate crystal precipitation, as little as a 20 per cent rise in urinary oxalate concentration resulted in calcium oxalate crystal forma-

tion.[24] Similarly, Finlayson has determined that the oxalate concentration has a 1.5-fold greater effect on calcium oxalate solubility than does the calcium concentration.[11] It would appear that in jejunoileal bypass patients, the manipulation of urinary oxalate concentration would be of potentially greater benefit than attempts to decrease urinary calcium.

Urinary oxalate concentration in the jejunoileal bypass patient is dependent upon enteric absorption and urine volume. While low-oxalate or oxalate-free diets will reduce urinary oxalate levels to normal, the regimen is unpalatable.[14] Furthermore, to expect adherence to a strict diet from patients previously incapable of compliance with any dietary program is unrealistic. Similarly, attempts to decrease oxalate absorption by using a low fat diet alone have also been unsuccessful.[14]

Urine volume is important in decreasing the oxalate concentration. Urine volumes of 2 to 4 liters are associated with decreased oxalate concentration; however, when urinary output falls below 2 liters, the oxalate concentration curve manifests a sharp increase. Ideally, the patient with a bypass should imbibe enough fluid to ensure a urine output of 3.6 liters daily.[11] Unfortunately, a high fluid intake in these patients is often accompanied by an increase in diarrhea.

In order to decrease urinary oxalate concentration, many investigators have sought to augment the amount of insoluble intestinal oxalate through pharmacologic means. Cholestyramine, 4 gm four times a day, and calcium carbonate, 0.84 gm four times a day, have both been used to precipitate ingested oxalate.[3, 6, 14] Reports concerning the benefits of these agents are conflicting. While Gregory noted only minimal improvement in microscopic stone-forming parameters in 32 jejunoileal bypass patients given either cholestyramine or calcium carbonate for three months, we have reported the absence of any symptomatic stone disease in a group of 36 jejunoileal bypass patients adhering to an immediate postoperative regimen of 0.84 gm of calcium carbonate three times a day over a 1½ to 2 year period.[6, 14] Stauffer and associates have shown that urinary oxalate concentration is directly related to the ratio of dietary oxalate to dietary calcium in patients with ileal resections ranging from 30 to 150 cm. In these studies, administration of up to 3 gm of calcium per day resulted in reductions of urinary oxalate to normal levels.[27] Furthermore, Barilla has shown that the simultaneous ingestion of calcium and magnesium with an equimolar amount of oxalate was capable of normalizing urinary oxalate excretion over an eight hour period. This regimen was also capable of blunting the usual postprandial peak in the urinary oxalate level.[1] The importance of these findings has been stressed by Finlayson who noted that urinary oxalate levels are most likely to exceed the concentration necessary to form crystals during the early postprandial period when oxalate absorption reaches a peak.[11] Once these seed crystals are formed, their growth continues, secondary to the continued supersaturation of urine with respect to calcium oxalate.

Another drug reported to be of value in treating absorptive hyperoxaluria is diethylaminoethanol cellulose, which acts as an anion exchanger to form an insoluble cellulose oxalate complex. Pinto reported the first group of 22 patients with absorptive hyperoxaluria who were returned to normal urinary oxalate levels while on treatment over a 6 to 26

month period. Aside from occasional constipation, no ill effects were associated with the drug.[23] Similar studies with bypass patients have yet to be reported.

Aside from regulating stone formation by decreasing the urinary concentration of oxalate, it is also possible to approach the problem by seeking to increase the urinary concentration of substances known to inhibit calcium oxalate crystallization: magnesium oxide (600 mg orally twice a day), pyrophosphate (500 mg orally three times a day), and methylene blue (100 mg orally three times a day).[1, 28, 32] The urinary concentration of magnesium in the bypass patient is often low. While Barilla noted a beneficial effect of magnesium and calcium administered to his bypass patients, Gregory, using 400 mg of magnesium oxide orally given twice a day over a three month period, found no significant change in hyperoxaluria.[1, 14] The studies of Takasaki suggest that rather than reliance on the separate absolute concentration of magnesium and of calcium in the urine, the ratio of urinary magnesium to urinary calcium was more predictive of possible continued stone formation. Patients with ratios of less than 0.01 often were noted to have recurrent stone disease.[29] While the use of pyrophosphates and methylene blue to inhibit calcium oxalate crystallization has been beneficial among calcium oxalate stone formers in the general population, their effectiveness in the jejunoileal bypass population has yet to be documented.

SUMMARY

Symptomatic calcium oxalate renal stones will form in approximately 11 per cent of patients undergoing jejunoileal bypass. Fortunately, the vast majority will pass a single stone; however, approximately 20 per cent of all stone-forming patients will require an open surgical procedure. Abdominal roentgenograms and intravenous pyelograms are necessary to detect clinically silent, albeit active, stone disease in the early postoperative years.

An increase in the soluble oxalate pool available for passive colonic absorption is responsible for acquired hyperoxaluria in the jejunoileal bypass patient. An optimal regimen to prevent hyperoxaluria would include a low fat, low oxalate diet, combined with high fluid intake. In addition, we propose the use of calcium carbonate or similar agents (cholestyramine or diethylaminoethanol cellulose) to precipitate oxalate within the bowel, thereby precluding its colonic absorption.

Increased vigilance on the part of the surgeon and the patient's adherence to a specific dietary and pharmacologic regimen are essential to the management of oxalate urolithiasis. With these measures the occurrence of calcium oxalate stone disease in jejunoileal bypass patients may decrease to a level commensurate with the general population.

REFERENCES

1. Barilla, D. E., Notz, C., Kennedy, B. S., et al.: Renal oxalate excretion following oral oxalate loads in patients with ileal disease and renal and absorptive hyperoxaluria. Am. J. Med., 64:579, 1978.

2. Caspary, W. F.: Enteric hyperoxaluria. New Engl. J. Med., *296*:1357, 1977.
3. Caspary, W. F., Tonissen, J., and Lankisch, P. G.: Enteral hyperoxaluria, effect of cholestyramine, calcium, neomycin, and bile acids on intestinal oxalate absorption. Acta Hepatogastroenterol., *24*:193, 1977.
4. Chadwick, B. S., Modha, K., and Dowling, R. H.: Mechanism for hyperoxaluria in patients with ileal dysfunction. New Engl. J. Med., *289*:172, 1973.
5. Chadwick, B. S., Modha, K., and Dowling, R. H.: Pathogenesis of secondary hyperoxaluria in ileal resection. Gut, *13*:840, 1972.
6. Clayman, R. V., Buchwald, H., Varco, R. L., et al.: Urolithiasis in patients with a jejunoileal bypass. Surg. Gynecol. Obstet., *147*:225, 1978.
7. DeWind, L. T., and Payne, J. H.: Intestinal bypass surgery for morbid obesity—long term results. J.A.M.A., *236*:2298, 1976.
8. Dickstein, S. S., and Frame, B.: Urinary tract calculi after operation for obesity. Surg. Gynecol. Obstet., *136*:257, 1973.
9. Earnest, D. L., Johnson, G., Williams, H. W., et al.: Hyperoxaluria in patients with ileal resections; an abnormality in dietary oxalate absorption. Gastroenterology, *66*:1114, 1974.
10. Fikri, E., and Cassella, R. R.: Jejunoileal bypass for massive obesity. Ann. Surg., *179*:460, 1974.
11. Finlayson, B.: Renal lithiasis in review. Urol. Clin. North Am., *1*:181, 1974.
12. Gelbart, D. R., Brewer, L. L., Fajardo, L. F., et al.: Oxalosis and chronic renal failure after intestinal bypass. Arch. Intern. Med., *137*:239, 1977.
13. Gourlay, R. H., and Reynolds, C.: Complications of surgery for morbid obesity. Am. J. Surg., *136*:54, 1978.
14. Gregory, J. G., Park, K. Y., and Schoenberg, H. W.: Oxalate stone disease after intestinal resection. J. Urol., *117*:631, 1977.
15. Halverson, J. D., Wise, L., Wazna, M. F., et al.: Jejunoileal bypass for morbid obesity, a critical appraisal. Am. J. Med., *64*:461, 1978.
16. Hofmann, A. F., Thomas, P. J., Smith, L. H., et al.: Pathogenesis of secondary hyperoxaluria in patients with ileal resection and diarrhea. Gastroenterology, *58*:960, 1970.
17. Hylander, E., Jarnum, S., Jensen, H. J., et al.: Enteric hyperoxaluria: dependence on small intestinal resection, colectomy, and steatorrhea in chronic inflammatory bowel disease. Scand. J. Gastroenterol., *13*:577, 1978.
18. Jewell, W. R., Hermreck, A. S., and Hardin, C. A.: Complications of jejunoileal bypass for morbid obesity. Arch. Surg., *110*:1039, 1975.
19. Mersheimer, W. L., Kazarian, K. K., and Durs, J. F.: A critical analysis of 51 patients with jejunoileal bypass. Surg. Gynecol. Obstet., *145*:847, 1977.
20. Miller, M. J., Frame, B., and Parfitt, A. M.: Nephrocalcinosis in intestinal bypass patients. Arch. Intern. Med., *137*:1743, 1977.
21. O'Leary, J. P., Thomas, W. C., Jr., and Woodward, E. R.: Urinary tract stone after small bowel bypass for morbid obesity. Am. J. Surg., *127*:142, 1974.
22. Payne, J. H., and DeWind, L. T.: Surgical treatment of obesity. Am. J. Surg., *118*:141, 1969.
23. Pinto, B., and Bernshtam, J.: Diethylaminoethanol-cellulose in the treatment of absorptive hyperoxaluria. J. Urol., *119*:630, 1978.
24. Robertson, W. G., Peacock, M., and Nordin, B. E. C.: Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. Clin. Sci., *40*:365, 1971.
25. Salmon, P. A.: The results of small intestine bypass operations for the treatment of obesity. Surg. Gynecol. Obstet., *132*:965, 1971.
26. Scott, H. W., Jr., Dean, R. H., Shull, H. J., et al.: Results of jejunoileal bypass in two hundred patients with morbid obesity. Surg. Gynecol. Obstet., *145*:661, 1977.
27. Stauffer, J. Q., Stewart, R. J., and Bertrand, G.: Acquired hyperoxaluria; relationship to dietary calcium content and severity of steatorrhea. Gastroenterology, *66*:783, 1974.
28. Sutor, D. J.: The possible use of methylene blue in primary hyperoxaluria. Brit. Med. J., *42*:389, 1970.
29. Takasaki, E.: Urinary magnesium and oxalic acid excretion in patients with recurrent oxalate urolithiasis. Invest. Urol., *12*:251, 1975.
30. Telmos, A. J.: Long-term morbidity of jejunoileal bypass. Am. Surgeon, *43*:389, 1977.
31. Thomas, M., and Madura, J.: Urolithiasis after intestinal bypass for morbid obesity. Urology, *9*:170, 1977.
32. Thomas, W. C., Jr.: Medical aspects of renal calculous disease—treatment and prophylaxis. Urol. Clin. North Am., *1*:261, 1974.

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The Liver in Morbid Obesity and Following Bypass Surgery for Obesity

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Morbidly obese individuals (those more than 100 pounds over ideal weight) have pathologic liver changes as part of their health burden.[56] This information has been known for many years, but it has been fully appreciated only after demonstration of the hepatic changes that follow jejunoileal bypass.

In the 1960s, surgical treatment of morbid obesity became an established and relatively accepted procedure. At first, jejunocolic then jejunoileal bypasses were constructed. With the appearance of abnormalities in the liver function and, especially after jejunocolic bypass hepatic failure, the liver function and structure of morbidly obese patients, before and after operative intervention, were examined. Unlike previously described groups of patients with "fatty liver," or fatty metamorphosis of the liver, this cohort was homogeneous. The patients were obese, they did not have diabetes, and those who used alcohol or other drugs had, for the most part, been excluded.

This article considers liver function tests and hepatic morphology in the morbidly obese before and after bypass surgery.

LIVER FUNCTION TESTS IN MORBIDLY OBESE PATIENTS

Most investigators report minimal abnormalities in liver function tests of obese patients before jejunoileal or gastric bypass.[6–8, 10, 40, 46, 52, 53, 55, 56]

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Table 1. *Percentage of Abnormal Liver Function Tests in Obese Patients*

TEST	TOTAL NO.	NO. ABNORMAL	PER CENT
SGOT	173	13	7.5
Alkaline phosphatase	202	17	8.4
Bilirubin	205	8	3.9
Serum albumin	212	32	15.1

The serum glutamic oxaloacetic transaminanse (SGOT) level was abnormal in 7.5 per cent of our patients (12/173), the alkaline phosphatase value was abnormally elevated in 8.4 per cent (17/202), the serum bilirubin level was abnormally elevated in only 3.9 per cent (8/205), and serum albumin values were less than 3.3 gm per 100 ml in 15 per cent (32/212) (Table 1).

PREBYPASS LIVER STRUCTURE

Most of these morbidly obese patients had liver biopsies at the time of intestinal bypass.[8, 25, 46, 52] The majority of these reports emphasize (1) fat in the hepatocytes, (2) portal fibrosis, and (3) portal infiltrates.

Fat

Fatty infiltration of the liver was found in 68 per cent of our original series,[28] in 94 per cent of Kern's patients,[25] and in 81 per cent (283 of 351) in our current series.[8] These lipid deposits vary from several small droplets of fat in centrolobular cells, to single, large droplets of fat, to a single droplet of fat formed in each hepatocyte in the biopsy; fat is not primarily distributed peri-portally. Our original experience with 88 patients and two years follow-up is summarized in Table 2. Originally, one third of the patients had no fat; the remaining patients were approximately equally divided among three groups corresponding roughly to mild, moderate, and severe fatty infiltration.

Holzbach et al. published the results of chemical analysis of the lipid content of the liver in morbid obesity.[22] The primary hepatic lipid that increased is triglyceride, whereas phospholipid, cholesterol, and free cholesterol levels are normal (Table 3).

Table 2. *Percentage of Hepatocytes Containing Fat*

	NEEDLE BIOPSIES PERFORMED	0%	< 25%	25–50%	> 50%
At Surgery	82	32	23	20	26
1 Year	68	5.9	27	28	44
2 Years	21	4.8	33.2	43	19

Table 3. *Lipid Content of the Liver (mg/gm) in Morbidly Obese Patients (± 1 S.D.)*

	AT SURGERY	1 YEAR POSTSURGERY
Total Lipid	110.7 ± 62.8	221.7 ± 180.2
Triglyceride	79.9 ± 63.3	117.2 ± 151.2
Phospholipid	23.8 ± 4.5	28.0 ± 12.1
Cholesterol, free	2.64 ± 3.66	2.5 ± 3.24
Cholesterol, esters	1.94 ± 3.68	2.25 ± 3.44

From Holzbach, R. T., et al.: Hepatic lipid in morbid obesity. New Engl. J. Med., 290:296, 1974, with permission.

The triglyceride in the liver has the same fatty acid composition as that stored in the adipose tissue. Fat is stored in adipose tissue as triglyceride; when free fatty acids are needed, lipoprotein lipases split them from the triglyceride. The free fatty acids are carried in the blood to liver cells, where they are taken up and esterified in the endoplasmic reticulum with α-glycerophosphate to form triglyceride. In the endoplasmic reticulum and in the Golgi apparatus, the triglyceride is "packaged" with phospholipid and cholesterol to form very low density lipoprotein, which is then transported from the liver in the hepatic venous blood. Lipoprotein lipases make free fatty acids available from the very low density lipoprotein for cellular metabolism.

In the absence of insulin, as in the fasting state, or in obesity, in which insulin resistance is found in fat cells, peripheral lipolysis is increased. The excess of hepatic triglyceride over phospholipid and cholesterol suggests that this relative lack of phospholipid and cholesterol interferes with very low density lipoprotein formation, thus blocking removal of triglyceride from the liver.[13]

Portal Tract Changes

Portal fibrosis and portal tract inflammation (inflammatory or mononuclear infiltration of the portal triad, "triaditis") are frequently noted. Kern et al. reported that 28 per cent of their patients had fibrosis; in 5.3 per cent it was either "moderate" or "severe," and 58 per cent had some degree of "triaditis."[26] They found Laennec's cirrhosis in 2 per cent (3 of 151) and "early cirrhosis" in 2 per cent, even though ethanol abuse had been excluded in their patients.

We found portal fibrosis in 9.8 per cent and portal round cell infiltrates in 19.6 per cent of our patients at the time of surgery. Biliary ductular proliferation was noted in 12.5 per cent but was usually minimal. None of our patients had either portal-central linkage or established micronodular cirrhosis (Table 4). Centrolobular, pericellular fibrosis was prominent in 8.5 per cent (7 of 82). This was similar to the central pericellular fibrosis seen in alcoholic hepatitis, but other features of this disease, i.e., Mallory's hyaline, central hyaline sclerosis, and central inflammation, were not seen. Thus, the central pericellular fibrosis in our morbidly obese patients did not seem to be the same lesion as that of alcoholic hepatitis. No patient in our group had cirrhosis or portal-central linkage at the time of surgery.

Table 4. *Portal Tract Changes in 38 Obese Patients*

CONDITION	PER CENT INITIALLY	AFTER 4 YEARS
Portal fibrosis	9.8	31.9
Portal infiltrate	19.6	42.0
Bile ductular proliferation	14.6	46.0
Central pericellular fibrosis	8.5	47.8
Portal-central linkage	0	6.8
Regenerative nodules	0	3.4

Correlation Between Preshunt Liver Function Tests and Morphology

Galambos and Wills attempted to correlate 505 paired liver function tests with 242 intraoperative liver biopsies in 242 obese patients who were to have jejunoileal bypass.[16] They found very poor "association between the abnormalities of the commonly used liver tests and moderate or severe lesions in liver biopsy." This was as true after bypass as before, which led them to conclude that liver biopsies should be done to determine hepatic status regardless of the results of liver function tests, a conclusion with which we concur.

LIVER CHANGES AFTER DIET THERAPY

Although we are interested primarily in the effects of small bowel and gastric bypass upon the liver, for control observations, the effects of dieting will be considered first.

Total Starvation

Rozental et al. studied five patients before, during, and after 14- to 30-day periods of starvation; their weights ranged from 110 to 217 kg.[47] Bromsulphalein retention was most markedly changed, with as much as 50 per cent retention in some, but SGOT, alkaline phosphatase, and even serum albumin levels changed very little. In two of the five biopsies taken before starvation there was a pericellular lattice of Masson-positive material similar to the findings in 8.6 per cent of our patients.

Verdy found similar changes in bromsulphalein retention in 28 patients but noted an early rise in SGOT and serum glutamic pyruvic transaminase with starvation that returned to normal after one week.[54] Examining biopsies taken 49 to 109 days after starvation was begun, Drenick et al. noted a marked reduction in fatty infiltration; bile stasis occurred in four of the 11 patients, and focal necrosis was increased.[12] Patients on a 500-calorie diet for an extended period of time had less fat in the liver than patients in the starved group. Biopsies taken from patients from these two groups (starved and dieted) who maintained their weight for up to five years were normal, the fat having cleared from the liver. The authors

concluded that mobilization of fat during weight reduction is not injurious to the liver.

SMALL BOWEL BYPASS

JEJUNOCOLIC BYPASS

Early in the development of small intestinal bypass surgery for obesity, when a jejunocolic bypass operation was being done, hepatocellular failure was found to be a major complication. At that time, preshunt liver biopsies were not performed routinely, and liver function was usually followed up by tests of bromsulphalein retention and alkaline phosphatase and SGOT levels. Two reports on groups of 10[40] and 11[53] patients suggested that these "liver function tests were either normal (alkaline phosphatase, serum transaminase) or borderline high (bromsulphalein) preshunt, but that after jejunocolic bypass, all three tests became abnormal in at least 50 per cent of patients." However, after six months they began to return to normal. This seemed to parallel a stabilization in weight, although the maintenance of flat results in glucose tolerance tests and low serum carotene levels[53] suggested continued malabsorption.

In a minority of patients, liver dysfunction became much worse than the relatively nonspecific changes previously discussed would suggest. Although there are not sufficiently large series to justify calculating percentages, five cases of hepatocellular failure and eventual death after jejunocolic bypass were reported for 63 patients (Table 5).

Bondar[5] and Maxwell[31] note that at autopsy their patients had only a fatty liver, without evidence of cirrhosis, and Shibata et al.[53] stated that their patients had fatty changes with a chronic portal inflammation. Shagrin et al. do not detail the two liver deaths they mention.[50] Delena et al. recognized that "taking down" a jejunocolic shunt with reestablishment of bowel continuity might stop the progression of hepatic dysfunction.[11]

Table 5. *Number of Deaths due to Hepatic Failure after Jejunocolic Shunts (1963 to 1971)*

REFERENCE	NO. OF PATIENTS	NO. OF DEATHS
Payne et al.[40]	10	0
Lewis and Turnbull[27]	11	0
Bondar and Pisesky[5]	7	1
Shibata et al.[53]	11	1
Maxwell et al.[31]	1	1
Shagrin et al.[50]	22	2
Total	62	5

In follow-up biopsies, Shibata[52] comments upon pericentral fibrosis yielding a fine central scarring. On electron microscopic study, collagen formation was seen in the spaces of Disse.

Jejunoileal Bypass

Liver Function Tests

Following small bowel bypass, there is a temporary rise then a return to normal of the serum transaminase and alkaline phosphatase levels and bromsulphalein retention in most patients. This is illustrated in Figures 1 and 2 and in Table 6, which present data from 300 patients seen between 1970 and 1978. The elevation was maximal in the first three months and returned toward normal by 12 months. This paralleled maximum weight loss.

Although 95 per cent of patients who have had jejunoileal bypass do well, approximately 5 per cent show deterioration of liver function as measured by a rising serum bilirubin value, ascites, and hepatic encephalopathy. Ten of 604 patients reported in the literature died of hepatic failure (Table 7). Our own experience is that although about 5 per cent of patients develop clinical and "biochemical" liver failure, with vigorous treatment only about 0.5 per cent will die of liver failure.

Liver Morphology

Liver biopsies taken one and two years after jejunoileal bypass in 88 patients showed the changes noted in Tables 2 and 4.[28] As had others, we found that the percentage of patients having fat in the liver increased

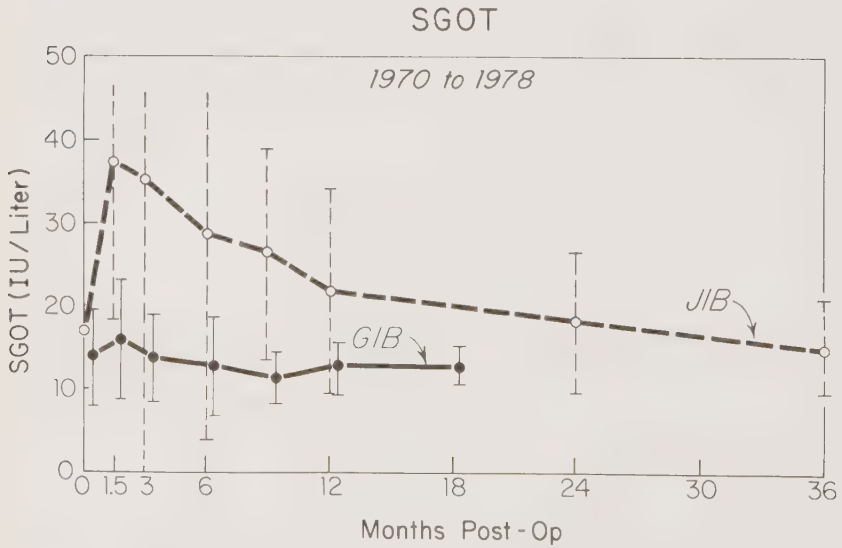

Figure 1. Sequential SGOT values after jejunoileal bypass (JIB) and gastric bypass (GIB).

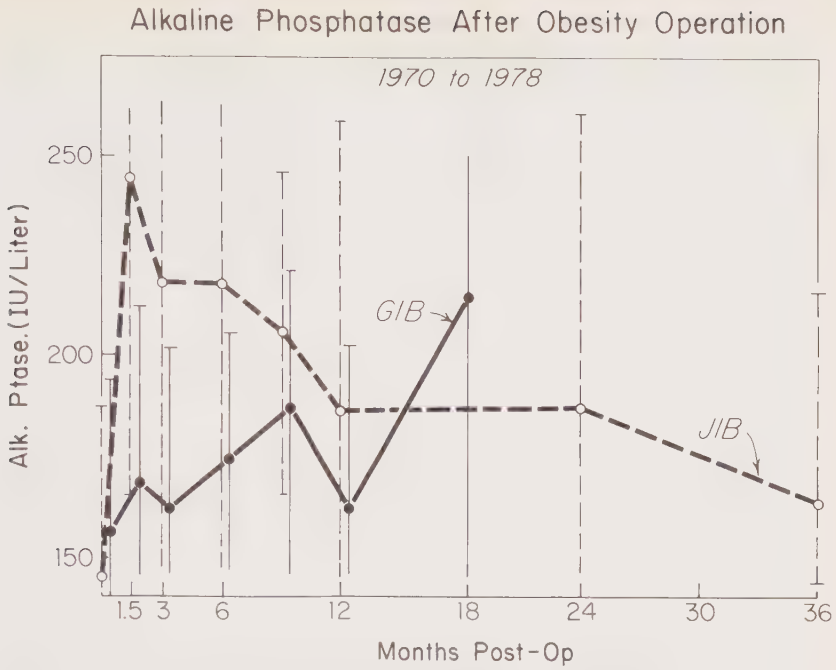

Figure 2. Sequential alkaline phosphatase values after jejunoileal bypass (JIB) and gastric bypass (GIB) are depicted in this chart.

after bypass, with only 5 per cent of the biopsies being free of fat at one and two years. However, by two years, the percentage of hepatocytes containing fat fell as weight stabilized.

All the abnormal findings noted before bypass were more frequent one year after bypass (see Table 4). It is significant that the presence of portal fibrosis, portal infiltration with inflammatory cells, or biliary proliferation

Table 6. *Results of Liver Function Tests after Jejunoileal Bypass in 300 Patients (1970 to 1978)*

	PRE-OPERATIVE (± S.D.)	1 YEAR POST-OPERATIVE (± S.D.)	PER CENT CHANGE	*p*
Total protein (gm %)	6.7 ± 0.5	6.3 ± 0.6	− 6.0	<0.001
Albumin (gm %)	3.6 ± 0.4	3.3 ± 0.5	− 8.3	<0.001
Prothrombin time (secs.)	10.6 ± 0.6	11.0 ± 1.0	+ 3.8	<0.001
Alkaline phosphatase (mμ/ml)	145.2 ± 42.2	185.9 ± 73.4	+28.0	<0.001
SGOT (mμ/ml)	17.1 ± 14.7	21.8 ± 12.3	+27.5	<0.001
Total bilirubin (mg %)	0.6 ± 0.3	0.8 ± 0.7	+25.0	<0.001
Cholesterol (mg %)	192.9 ± 39.4	113.2 ± 27.5	−41.3	<0.001
Triglycerides (mg %)	179.3 ± 143.4	114.8 ± 64.8	−36.0	<0.001

Table 7. *Number of Deaths due to Hepatic Failure after Jejunoileal Bypass (1971 to 1973)*

REFERENCE	NO. OF PATIENTS	NO. OF HEPATIC FAILURE DEATHS	NO. OF TOTAL DEATHS
Baddelley[4]	60	1	1
Weismann[55]	123	1	3
Baber et al.[3]	90	2	2
Payne et al.[41]	165	5	16
Brown et al.[6]	36	1	4
Salmon[48]	120	0	5
Juhl et al.[24]	10	0	0
Total	604	10 (1.7%)	31 (5.2%)

did not predict progression. These lesions disappeared after shunt in some patients and appeared in others. Progression and regression of portal fibrosis is illustrated in Figure 3.

The lesion that did predict invariable progression after bypass was central pericellular fibrosis. This begins near the central vein with the

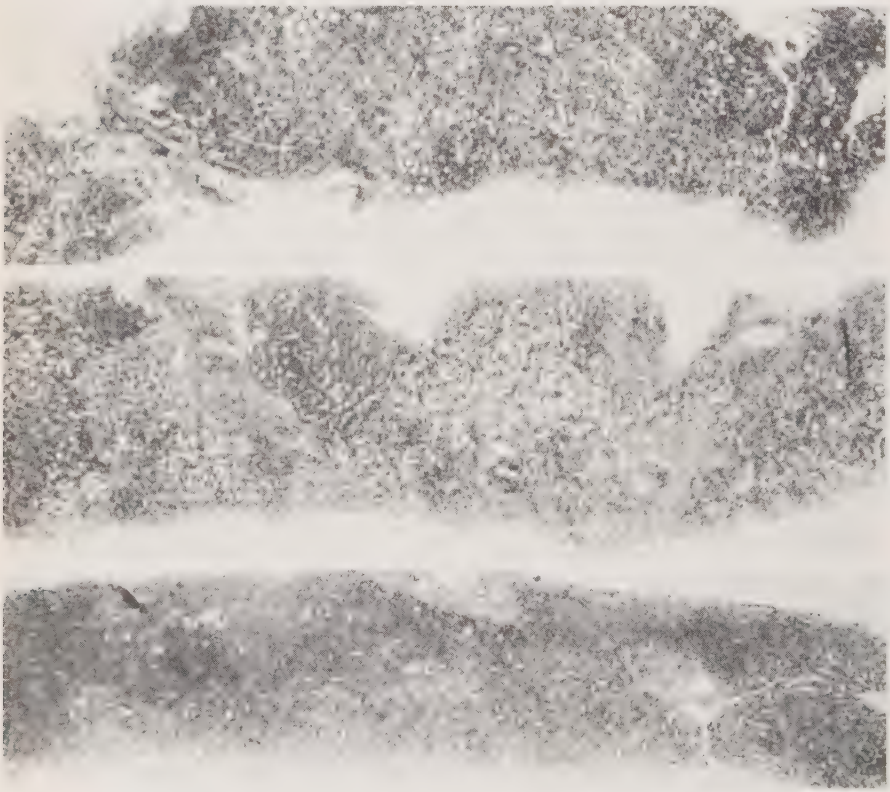

Figure 3. Liver biopsy in a jejunoileal bypass patient showing intraoperative presence of portal fibrosis prior to bypass (top), the progression of fibrosis by one year (middle), and the regression by two years (bottom). (Masson trichrome stain, × 25)

formation of collagen fibrils between the hepatocytes and the sinusoidal lining cells in the spaces of Disse. The collagen fibrils coalesce and become bundles of collagen surrounding the individual central hepatocytes (Fig. 4).[28] Electron microscopic examination of this area reveals basement membranes between the sinusoids and many of the hepatocytes (Fig. 5). Basement membranes are normally found only in the portal triads and in the central veins. Their presence in these regions is believed to interfere with the passage of oxygen and nutrients across the sinusoid into the hepatocytes.

Central pericellular fibrosis is directly analogous to the central lesion in alcoholic hepatitis[42, 43] and is thought to be the precursor lesion to a scar that links portal and central areas, subdividing the liver into the pseudolobules of micronodular cirrhosis.[17] In 6.8 per cent of the patients we described, the centrolobular pericellular "net" of collagen did extend from the central areas to link with the portal triad. Half of these patients developed regenerative cirrhotic nodules. None of these patients had had this lesion prior to bypass surgery.

McGill et al. described Mallory's hyaline in a patient who developed hepatic failure after jejunoileal bypass.[33] Three years later, Peters et al. reported five patients who developed Mallory's hyaline after bypass.[43] Two of these five had lesions similar in every degree to those of patients with alcoholic hepatitis. In only one of the 250 biopsies we have studied did a lesion mimicking alcholic hepatitis develop. Mallory's hyaline was somewhat more frequent in our patients, but it occurred in very small amounts and might have been in periportal areas as well as in the central area. When Mallory's hyaline is present in alcoholic liver disease, it is almost

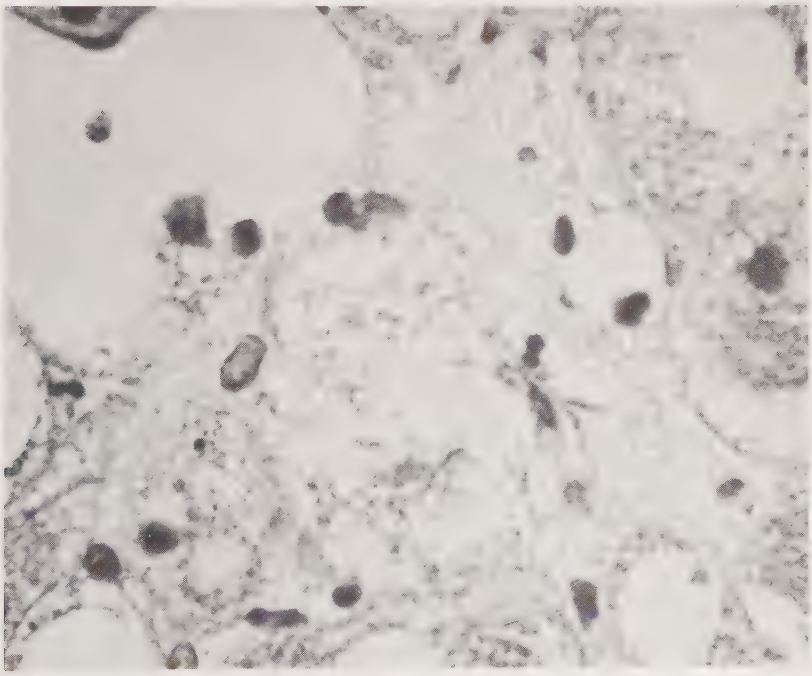

Figure 4. Characteristic lesion of central pericellular fibrosis. (Azo-carmine stain, × 400).

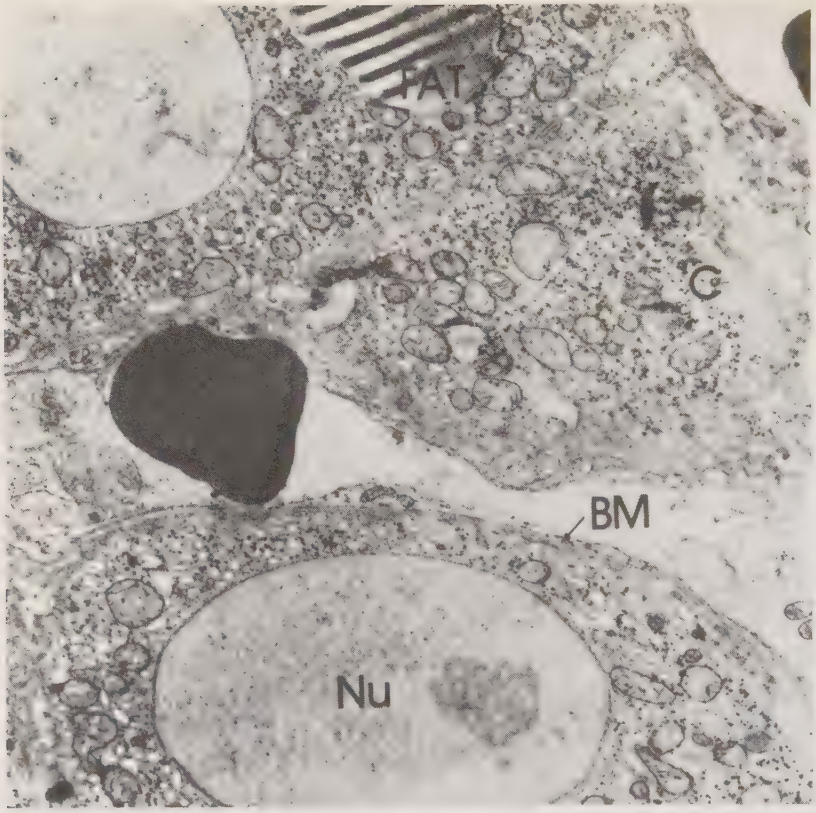

Figure 5. Electron micrograph showing early basement membrane (BM) formation characteristic of the origin of central pericellular fibrosis.

always centrolobular and in generous amounts. A lesion resembling that of alcoholic hepatitis is very uncommon after jejunoileal bypass, and when it occurs, one must be very certain to exclude alcohol as its true cause.

In addition to the changes in collagen production and basement membrane development, electron microscopic studies have shown enlarged mitochondria in the periportal hepatocytes—those with the least fat accumulation.[15, 44] Periportal mitochondrial cristae and paracrystalline inclusions increased—the amount roughly paralleling the amount of central fat. The liver oxidizes most of its fatty acids in the mitochondria[13] and it has been suggested that mitochondrial function, and therefore structure, was modified because of the increased intracellular fat.[15, 44]

A less frequent lesion has been the development of chronic active hepatitis reported by Peters.[42] We have seen this occur once. It may be coincidental or part of the spectrum of this disease.

Hepatic granulomata have been reported by Halvorson et al.[19] in up to 7 per cent of patients; we, too, have seen these changes.

In those patients who die in hepatic failure, cirrhosis, focal necrosis, cholestasis, and Mallory's hyaline have been found.[33, 43] Some of these

Table 8. *Results of Liver Function Tests after Gastric Bypass in Morbidly Obese Patients (1976 to 1978)*

	PREOPERATIVE (±S.D.)	1 YEAR POSTOPERATIVE (±S.D.)	PER CENT CHANGE	*p*
Total protein (gm %)	7.0 ± 0.5	6.9 ± 0.8	− 1.4	NS
Albumin (gm %)	3.7 ± 0.3	3.9 ± 0.4	+ 5.4	NS
Prothrombin time (secs.)	10.7 ± 0.6	11.1 ± 0.9	+ 3.7	NS
Alkaline phosphatase (mμ/ml)	156.0 ± 37.6	162.2 ± 41.8	+ 4.0	NS
SGOT (mμ/ml)	13.2 ± 6.4	12.4 ± 3.1	− 6.1	NS
Total bilirubin (mg %)	0.5 ± 0.3	0.4 ± 0.3	−20.0	NS
Cholesterol (mg %)	195.5 ± 29.8	175.2 ± 31.3	−10.4	0.05
Triglycerides (mg %)	182.2 ± 105.4	137.0 ± 94.4	−24.8	NS
N	56 to 61	6 to 14		

patients seemed to be relatively well, if somewhat weak, until shortly before going into acute failure and death. The morphologic changes may be poorly associated not only with the laboratory tests but also with the clinical appearance of the patient.

GASTRIC BYPASS

Liver Function Tests

Results of liver function tests in our patients who have had a gastric bypass for obesity (Table 8, Figs. 1 and 2) are similar to those of patients who dieted. One year after gastric bypass, the tests are essentially unchanged.

Liver Morphology

The same preoperative morphology that has been described in jejunoileal bypass patients has been reported in gastric bypass patients.[1, 9, 18, 30] Both Mason and Printen[29] and Alden[1] stated that repeat biopsies during follow-up showed either no change or an improvement in hepatic morphology. Griffen et al. showed no change in 2 and improvement in 10 of 12 gastric bypass patients rebiopsied at one year.[18] Buchwalter demonstrated no change in three and improvement in three of six patients at one year.[9]

We are currently analyzing the sequential liver morphology on biopsy in our series of gastric bypass patients at one and two years. These data will be available in the near future.

CAUSES OF LIVER FAILURE

The cause of liver failure after jejunoileal bypass is not known. Plausible theories postulate (1) protein deficiency,[21, 36] (2) circulating endotoxin produced by bacterial overgrowth in the bypassed segment of ileum or

lithocholic acid toxicity,[12] and (3) stimulation of hepatic proline collagenase.[14]

Because liver failure seems to occur most often (or perhaps only most noticeably) in patients experiencing rapid and excessive weight loss, and because Moxley et al.[36] documented amino acid profiles characteristic of protein deficiency following jejunoileal bypass, a theory of relative protein deficiency with protein-fat imbalance has held the greatest interest. As a rule, patients who undergo this surgery eat unwisely and usually consume a diet high in fat and carbohydrate. Part of treatment, preferably prophylactic, is to teach them to modify this habit, adding protein and reducing the fat in their diet; this is not always successful. That many have been able to reverse jaundice and early liver failure with protein supplementation by mouth, jejunal feeding tube, or parenteral hyperalimentation lends credence to the theory of relative protein deficiency.

Since protein deficiency does not result in cirrhosis in kwashiorkor, a classic protein deficiency disease in which there is a massively fatty liver, many have questioned protein deficiency as the sole etiology of liver failure after jejunoileal bypass.[45] Some have postulated endogenous alcohol production;[34] a role for bile acids, especially lithocholic acid;[35, 39, 51] and a factor stimulating hepatic proline collagenase.[14]

Endotoxin production by bacteria growing in the bypassed small bowel segment, with circulation of the endotoxin through the portal vein to the liver, has been suggested[37, 38] and may represent the necessary "extra factor." In the reported experiments, bacteroides growing in the bypassed loop seemed to cause liver failure in dogs. When the small bowel segment was either removed, rather than bypassed, or sterilized by antibiotics, liver failure did not result. Antibiotics have been of some help in humans but not as successful as the dog model might suggest.

TREATMENT OF LIVER DISEASE AND FAILURE

Clinical liver failure most often appears between 3 and 12 months after surgery. Rarely has it appeared after 24 months. When weakness, hypoalbuminemia, and hypoprothrombinemia occur, and before the onset of clinical jaundice, intensive treatment is required. Various regimens recommended include antibiotics,[49] high-protein supplements and hyperalimentation with amino acids,[20] tube feedings and jejunostomy feedings,[32] and finally reanastomosis.

Scott et al. advocate use of metronidazole, tetracycline, or doxycycline, together with elemental dietary supplements.[49] If the patient does not respond quickly to this therapy, take-down of the jejunoileal bypass is advised.

McClellan et al. reported that in dogs, liver failure after jejunoileal bypass could be prevented without affecting weight gain by giving medium chain triglycerides or predigested gelatin by jejunostomy into the bypassed loop.[32] Our results with a limited number of patients do not show as good a response with feeding jejunostomies.

Ames[2] and Heimburger[20] both report reversal of liver function abnormalities and improvement of the amount of fat in the liver by intravenous hyperalimentation.

Revision of the jejunoileal bypass is usually the last treatment tried and follows attempts to reverse liver failure with protein, antibiotics, and other measures. In the 1977 survey of 1139 patients reported by Iber and Cooper,[23] 10.7 per cent were reversed (122 patients), 4.1 per cent (47) because of liver failure. About one half of the patients who had the bypass reversed for liver failure improved; the others deteriorated and died. Perhaps earlier intervention would have been indicated, but most patients have so much invested emotionally in this procedure, that they resist suggestion to reverse the shunt. In our series of jejunoileal bypass patients, we have had a 5 per cent liver failure rate and a 1 per cent need for take-down, generally followed by full patient recovery. The performance of a concurrent gastric bypass at the time of take-down has markedly improved our total patient care and has persuaded patients to allow earlier reestablishment of small bowel continuity for significant complications.

CONCLUSIONS

Obviously, it is better to prevent liver failure than to treat it. Thus, we have two suggestions for jejunoileal bypass surgeons. First, patients should be indoctrinated preoperatively and postoperatively regarding the need to eat normal or more than normal amounts of protein to prevent the protein-calorie-fat imbalance that may be critical in the development of liver failure. Second, candidates for this surgery should have a preoperative needle biopsy of the liver. Those with centrolobular fibrosis or frank cirrhosis should be excluded from consideration for a jejunoileal bypass (a gastric bypass could probably be performed as an alternative), inasmuch as their lesions will probably progress.

REFERENCES

1. Alden, J.: Gastric and jejunoileal bypass: A comparison in treatment of morbid obesity. Arch. Surg., *112*:799, 1977.
2. Ames, G. C., Copeland, E. M., Leeb, D. C., et al.: Liver dysfunction following small bowel bypass for obesity. Non-operative treatment of fatty metamorphosis with parenteral hyperalimentation. J.A.M.A., *235*:1249, 1976.
3. Baber, J. C., Hayden, W. F., and Thompson, B. W.: Intestinal bypass operations for obesity. Am. J. Surg., *126*:769, 1973.
4. Braddelley, R. M.: Surgical treatment of obesity. Proc. R. Soc. Med., *66*:1098, 1973.
5. Bondar, G. F., and Pisesky, W.: Complications of small intestinal short circuiting for obesity. Arch. Surg., *94*:707, 1967.
6. Brown, R. G., O'Leary, J. P., and Woodward, E. R.: Hepatic effects of jejunoileal bypass for morbid obesity. Am. J. Surg., *127*:53, 1974.
7. Buchwald, H., Lober, P. H., and Varco, R. L.: Liver biopsy findings in seventy-seven consecutive patients undergoing jejunoileal bypass for morbid obesity. Am. J. Surg., *127*:48, 1974.
8. Buchwald, H. Rucker, R. D., Varco, R. L., et al.: Liver changes in obesity and following obesity operations. *In* Najarian, J. S., and Delaney, J. P. (eds.):Gastrointestinal Surgery. Symposium Specialists, 1979, in press.

9. Buchwalter, J. A.: A prospective comparison of the jejunoileal and gastric bypass operations for morbid obesity. World J. Surg., *1*:757, 1977.
10. Campbell, J. M., Hunt, T. K., Karem, J. H., et al.: Jejunoileal bypass as a treatment for morbid obesity. Arch. Intern. Med., *137*:602, 1977.
11. Delena, S. A., Fechner, R. E., Brown, H., et al.: Reversible fatty liver with fibrosis following jejuno-colic shunt. South. Med. J., *63*:399, 1970.
12. Drenick E. J., Simmons, F., and Murphy, J. F.: Effect on hepatic morphology of treatment of obesity by fasting, reducing diet, and small bowel bypass. New Engl. J. Med., *282*:829, 1970.
13. Farber, E.: The liver in protein and lipid metabolism, *In* Gall, E. A. (ed.): The Liver. Baltimore, Williams and Wilkins Co., 1973.
14. Feinman, L., and Lieber, C. S.: Hepatic collagen metabolism: Effects of alcohol consumption in rats. Science, *176*:795, 1972.
15. Friedman, H. I., Chandler, J., and Nemeth, T. J.: Hepatic intramitochondrial filaments in morbidly obese patients undergoing intestinal bypass. Gastroenterology, 73:1353, 1977.
16. Galambos, J. T., and Wills, C. E.: Relationship between 505 paired liver biopsy tests and biopsies in 242 obese patients. Gastroenterology, *74*:1191, 1978.
17. Gerber, M. A., and Popper, H.: Relation between central canals and portal tracts in alcoholic hepatitis. Hum. Pathol., *3*:199, 1972.
18. Griffen, W. O., Jr., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. Ann. Surg., *186*:500, 1977.
19. Halvorson, J. D., Wise, L., Wazna, M. F., et al.: Jejunoileal bypass for morbid obesity. A critical appraisal. Am. J. Med., *64*:461, 1978.
20. Heimburger, S. L., Steiger, E., LoGerfo, P., et al.: Reversal of severe fatty hepatic infiltration after intestinal bypass for morbid obesity by calorie-free amino acid infusion. Am. J. Surg., *129*:229, 1975.
21. Holzbach, R. T.: Hepatic effects of jejunoileal bypass for morbid obesity. Am. J. Clin. Nutr., *30*:43, 1977.
22. Holzbach, R. T., Wieland, R. G., Lieber, C. S., et al.: Hepatic lipid in morbid obesity. New Engl. J. Med., *290*:296, 1974.
23. Iber, F. L., and Cooper, M.: Jejuno-ileal bypass for the treatment of massive obesity. Prevalence, morbidity and short- and long-term consequences. Am. J. Clin. Nutr., *30*:4, 1977.
24. Juhl, E., Christoffersen, P., Baden, H., et al.: Liver morphology and biochemistry in eight obese patients treated with jejuno-ileal anastomosis. New Engl. J. Med., *285*:543, 1971.
25. Kern, W. H., Heger, A. H., Payne, J. H., et al.: Fatty metamorphosis of the liver in morbid obesity. Arch. Pathol., *96*:342, 1973.
26. Kern, W. H., Payne, J. H., and DeWind, L. T.: Hepatic changes after small intestinal bypass for morbid obesity. Am. J. Clin. Pathol., *61*:763, 1974.
27. Lewis, L. A., and Turnbull, R. B., Jr.: Effects of jejuno-colic shunt on obesity, serum lipoproteins, lipids, and electrolytes. Arch. Intern. Med., *117*:4, 1966.
28. Marubbio, A. T., Jr., Buchwald, H., Schwartz, M. Z., et al.: Hepatic lesions of central peri-cellular fibrosis in morbid obesity and after jejuno-ileal bypass. Am. J. Clin. Pathol., *66*:684, 1976.
29. Mason, E. E., and Printen, K. J.: Gastric surgery for relief of morbid obesity. Arch. Surg., *106*:428, 1973.
30. Mason, E. E., Printen, K. J., Hartford, C. E., et al.: Optimizing results of gastric bypass. Ann. Surg., *182*:405, 1975.
31. Maxwell, J. G., Richards, R. L., and Acbo, D.: Fatty degeneration of the liver after intestinal bypass for obesity. Am. J. Surg., *116*:648, 1968.
32. McClellan, R. N., DeHazo, C. V., Heimback, D. M., et al.: Prevention of hepatic injury after jejunoileal bypass by supplemental jejunostomy feedings. Surg. Forum, *21*:368, 1970.
33. McGill, D., Humphreys, S. R., Baggenstoss, A. H., et al.: Cirrhosis and death after jejunoileal shunt. Gastroenterology, *63*:872, 1972.
34. Mezey, E., Imbembo, A. L., Potter, J. J., et al.: Endogenous ethanol production and hepatic disease following jejuno-ileal bypass for morbid obesity. Am. J. Clin. Nutr., *28*:1277, 1975.
35. Morrisey, K. P., McSherry, C. K., Swarm, R. L., et al.: Toxicity of chenodeoxycholate in the non-human primate. Surgery, *77*:851, 1975.
36. Moxley, R. T., Pozefsky, T., and Lockwood, D. H.: Protein nutrition and liver disease after jejuno-ileal bypass for morbid obesity. New Engl. J. Med., *290*:921, 1974.
37. Nolan, J. P.: The role of endotoxin in liver injury. Gastroenterology, *69*:1346, 1975.
38. O'Leary, J. P., Maher, J. W., Hollenbeck, J. I., et al.: Pathogenesis of hepatic failure after obesity bypass. Surg. Forum, 25:1974.
39. Palmer, R. H.: Bile acids, liver injury, and liver disease. Arch. Intern. Med., *130*:606, 1972.
40. Payne, J. H., DeWind, L. T., and Commons, R. R.: Metabolic observations in patients with jejuno-colic shunts. Am. J. Surg., *106*:273, 1963.

41. Payne, J. H., DeWind, L. T., Schwab, C. E., et al.: Surgical treatment of morbid obesity. Arch. Surg., *106*:432, 1973.
42. Peters, R. L.: Hepatic morphologic changes after jejuno-ileal bypass. *In* Popper, H., and Schaffner, F. (eds.): Progress in Liver Diseases, Vol. VI. New York, Grune and Stratton, 1979.
43. Peters, R. L., Gay, T., and Reynolds, T. B.: Post-jejunal bypass hepatic disease. Its similarity to alcoholic hepatic disease. Am. J. Clin. Pathol., *63*:318, 1975.
44. Petersen, P.: Abnormal mitrochondria in hepatocytes in human fatty liver. Acta Pathol. Microbiol. Scand. [A], *85*:413, 1977.
45. Popper, H., and Schaffner, F.: Nutritional cirrhosis in man? New Engl. J. Med., *285*:577, 1971.
46. Randolph, J. G., Weintraub, W. H., and Regg, A.: Jejuno-ileal bypass for morbid obesity in adolescents. J. Pediatr. Surg., *3*:341, 1974.
47. Rozental, P., Biava, C., Spencer, H., et al.: Liver morphology and function tests in obesity and during total starvation. Am. J. Dig. Dis., *12*:198, 1967.
48. Salmon, P. A.: The result of small intestine bypass operations for the treatment of obesity. Surg. Gynecol. Obstet., *132*:965, 1971.
49. Scott, H. W., Dean, R. H., Shull, H. J., et al.: Results of jejuno-ileal bypass in two hundred patients with morbid obesity. Surg. Gynecol. Obstet., *145*:661, 1977.
50. Shagrin, J. W., Frame, B., and Duncan, H.: Polyarthritis in obese patients with intestinal bypass. Ann. Intern. Med., *75*:377, 1971.
51. Sherr, H. P., Nair, P. P., White, J. J., et al.: Bile acid metabolism and hepatic disease following small bowel bypass for obesity. Am. J. Clin. Nutr., *27*:1369, 1974.
52. Shibata, H. R., Mackenzie, J. R., and Huang, S.: Morphologic changes of the liver following small intestinal bypass for obesity. Arch. Surg., *103*:229, 1971.
53. Shibata, H. R., Mackenzie, J. R., and Long, R. C.: Metabolic effects of controlled jejunocolic bypass. Arch. Surg., *95*:413, 1967.
54. Verdy, M.: BSP retention during total fasting. Metabolism, *15*:769, 1966.
55. Weismann, R. E.: Surgical palliation of massive and severe obesity. Am. J. Surg., *125*:437, 1973.
56. Zelman, S.: The liver in obesity. Arch. Int. Med., *90*:141, 1952.

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Gallstones, Obesity, and Jejunoileostomy

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It has been repeatedly observed,[7, 17, 27] with rare exceptions,[9] that obesity is a risk factor for the development of cholelithiasis. Patients undergoing jejunoileal bypass surgery for control of obesity have also been reported to have an increased susceptibility to gallstone formation.[48] Since the pathogenesis of stone formation may differ before and after bypass surgery, we will review the current concepts of gallstone formation. Since this increased risk is noted only for cholesterol gallstones, the discussion will be limited to this type.

There are theoretically three stages of cholesterol gallstone formation:[10] saturation of bile with cholesterol, crystallization of cholesterol molecules, and growth. Of these stages, the processes concerned with the formation of a saturated or supersaturated bile have been most extensively studied. The later stages of deposition of cholesterol crystals and their subsequent growth to macroscopic size are undoubtedly important, but are still not well understood.[7]

In man, cholesterol is excreted primarily through the biliary tract. Only a third is removed by conversion to primary bile acids, cholic and chenodeoxycholic acids, and subsequent excretion of these. Bile acids, along with phospholipids, are the main components of "micelles" which help keep the cholesterol in a soluble form in bile. The relationship between these substances can be expressed as the percentage molar concentration of bile, lecithin, and cholesterol on triangular coordinates.[1] From this, the "lithogenicity" of a bile specimen may be obtained. Another method is to calculate the lithogenic index,[32] the ratio of the *actual* amount of cholesterol present in the specimen to the maximum amount of cholesterol that can be dissolved in it. These indices are useful, although not absolute, indicators of saturated bile and of the tendency to cholesterol crystallization.[25]

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The source of "abnormal" bile is at present presumed to be the liver.[7, 41] The mechanics have not been worked out, but this process may be dependent upon cholesterol synthesizing enzymes (HMG CO-A reductase). Altered or decreased bile acid metabolism and pool size (normally 3 to 5 gm) have also been documented in some patients.[5] The excretion of phospholipid usually parallels that of bile salts, but phospholipid abnormalities have not been found to clinically affect gallstone formation in man. Crystallization of cholesterol is affected by factors such as mucoproteins, bacteria, and calcium ion, but their precise significance is still far from being understood. Finally, factors which allow the crystals to coalesce, such as calcium ion and stratification of gallbladder bile, are still being investigated.[4, 13]

Most autopsy and clinical surveys show that obesity is commonly associated with gallstones. The Framingham Study[32] showed a definite, though irregular, gradient of this risk with increasing weight, independent of other factors. In autopsy studies of individuals above the age of 20 years the prevalence of gallstones is about 11 per cent.[5] In obese patients being evaluated for bypass surgery, the incidence of stones present or previously operated upon range from 30 to 35 per cent.[14, 16, 28, 29, 31] It is also felt that there may be an association between obesity and gallstones in Pima Indians, although it is difficult to correlate them because both problems are very common in that population.[36]

Obese subjects have significantly increased saturation of their bile as compared to nonobese controls.[6, 30] This is believed to be the result of excessive hepatic secretion of cholesterol.[31, 39] In obese subjects the hourly excretion rates of cholesterol and phospholipids have been found to be significantly elevated whereas that of bile salts is normal or only mildly elevated. This is in contrast to the situation in "normal weight" patients with gallstones who have a normal excretion rate of cholesterol and a decreased rate of bile salt excretion.[47] Interestingly enough, if the excretion rates of cholesterol and bile acid are corrected for weight, the values approach those of nonobese patients, i.e., diminished bile salt pool size relative to cholesterol excretion. This has led Mabee et al.[30] to suggest that hepatic cholesterol excretion may be responsive to factors other than bile salt flow. The effects of obesity per se on ileal motility and/or reabsorption of bile salts may play a role, but there is so far no evidence of either excessive or decreased enterohepatic circulation of bile salts (7 or 8 cycles per day) which may lead to altered excretion of cholesterol. An increased synthesis of cholesterol in obesity with consequent increased secretion in bile has been shown to occur.[22, 33] Under this thesis, gallstones would not develop in patients in whom bile salt pools increase as well as cholesterol secretion.[19] This may be dependent, however, upon the type of bile acids and the lithogenic ratio.[34]

The source of excessive cholesterol secretion may be the liver, the intestines, or adipose tissue.[20] The role of HMG CO-A reductase, which helps in the conversion of HMG CO-A to mevalonic acid which is finally metabolized to cholesterol, has also been investigated. This enzyme appears to be the rate-controlling step in the synthesis of cholesterol. Greater than normal content of this enzyme has been found in liver biopsy speci-

mens from some patients with gallstones.[35] Elevated levels have also been found with increased caloric intake and plasma insulin, both of which have been noted in obese patients.[7] Because of uncertainties with regard to the assay of HMG CO-A reductase, it has been difficult to determine whether its role in hepatic biliary "saturation" is primary or not.

The role of diet and drugs in obese patients may also be important. A high caloric intake is associated with increased hepatic cholesterol secretion and, therefore, with the formation of a supersaturated bile. This effect is observable in both lean and obese persons, but is more marked in the obese.[37, 38] Certain drugs, such as clofibrate and cholestyramine, which may be used more often in obese patients, have also been found to be lithogenic. An increased number of patients were noted to be subjected to cholecystectomy after they had been taking clofibrate for control of their hyperlipidemia.[8, 21] Clofibrate is associated with increased biliary cholesterol saturation. It has been postulated that this is secondary to increased cholesterol mobilization from adipose tissue following the decrease in cholesterol synthesis which occurs with this agent. Decreased cholesterol synthesis, which is the precursor of bile salts, can also lead to decreased bile salt production and a relative lack of bile salts. Cholestyramine, on the other hand, binds bile acids. Its use has been associated with decreased levels of chenodeoxycholic and deoxycholic acid with a resultant increase in cholic acid. There has also been an increase in the glycine/taurine ratio which, as will be discussed later, leads to the formation of "lithogenic bile."[50]

Finally, it would be pertinent to note the effect of weight loss on bile metabolism, since most obese patients undergo periods of dieting. Hepatic bile saturation does not decrease with low caloric intakes in obese patients.[6] This may be the result of increased mobilization of cholesterol from the fat stores which, in turn, leads to increased biliary cholesterol excretion. This state of affairs usually lasts during the period of weight loss only, for once the weight stabilizes at a lower level less cholesterol is found in bile.[6]

EFFECT OF JEJUNOILEAL BYPASS FOR MASSIVE OBESITY UPON GALLSTONE FORMATION

The increased formation of gallstones following jejunoileostomy has been noted.[12, 14, 16, 18, 28, 40, 45, 48] The incidence of this condition has been variously reported as 13 to 30 per cent. An annual rate of risk of developing gallstones has been quoted as being up to 52 per cent, which is about twice the level calculated for similar obese patients without surgery. In fact, some authors[2] have recommended cholecystectomy at the time of bypass surgery, but this has not been universally accepted. In view of the variety of metabolic changes induced by jejunoileal bypass surgery, it is not surprising that bile acid and cholesterol excretion would be altered, thus affecting the formation of gallstones in these patients. Because of the reduction in ileal surface after jejunoileostomy the increased fecal loss of bile acids[16] should lead to a diminished bile salt pool and therefore to

increased formation of gallstones. This increase has been seen in patients with ileal disease.[23, 24, 46] The lithogenicity of bile specimens obtained postoperatively increases in the early postoperative (six weeks) period[3] but returns to preoperative levels by six to 12 months.[16] These levels may be lithogenic in some patients, however, so that the risk of stone formation continues. Patients in whom stones develop have a greater excretion of fecal bile acids and a greater fall in serum cholesterol, suggesting increased cholesterol mobilization and metabolism.[15] There is, however, a suggestion that the length of the remaining ileum may be important in determining "lithogenicity." Surprisingly, increased cholesterol saturation of bile was associated with decreased jejunal and increased ileal length (37.5 cm versus 12.5 cm).[42] In addition, the issue of bacterial overgrowth and consequent bile salt deconjugation must be considered since this may result in diarrhea and loss of bile salts.[11] A number of patients were found to harbor enterobacteria in the small intestine following bypass surgery. The bacterial transitional area in the intestine may be displaced to reach the jejunum and intestinal contents may reflux into the bypassed segment, resulting in bacterial growth similar to a blind loop. Of greater interest, however, are the changes in bile acids. Fecal cholic and deoxycholic acid increase postoperatively in comparison to chenodeoxycholic acid and lithocholic acid.[16] Cholic acid is believed to be produced more easily in periods of stress and it may be less efficient in solubilizing cholesterol. Another consistent finding has been an increase in the glycine/taurine ratio.[49] The stability of a micellar suspension in bile has been shown to depend upon the relative strengths of the physiochemical forces of the biliary lipids. Taurine has a negative sulfate group and strengthens micellar formation in comparison to glycine. The rise in glycine with less taurine conjugation, while readily indentifiable, is not easily explained.[48, 49] It may be the result of rapid formation and turnover of bile acids in these patients with taurine being less readily available for conjugation than glycine.

THERAPY AND PROPHYLAXIS

Since there is an increase, or no decrease, in the saturation of bile with cholesterol, at least up until 12 months after jejunoileostomy, and an increase in the rapidity (if not the frequency) of cholesterol stone formation, therapy or prophylaxis should be considered in these patients. How does one increase the bile salt pool and decrease the lithogenic or saturation index? Mok et al.[34] have demonstrated that chenodeoxycholic acid therapy can reduce the saturation index during weight loss in the *intact obese* patient. This raises the possibility of preventing the formation of gallstones during weight loss. Without weight loss, very large doses of chenodeoxycholic acid may be needed.[26]

The situation in the obese patient with a jejunoileostomy may be more complicated and the patient may be less responsive to chenodeoxycholic acid therapy. Such a patient is not only obese and losing weight (and mobilizing cholesterol), but also is reducing his bile salt pool markedly[43] by

increasing his fecal excretion of bile acids. During this period of weight loss, chenodeoxycholic acid may not be absorbed efficiently and may also enhance the diarrhea by adding to the bile acid irritant effect in the colon. Nevertheless, the effect of such prophylaxis (or therapy in the case of stones already present) needs to be investigated. Furthermore, the use of ursodeoxycholic acid, which is reported to produce less diarrhea than does chenodeoxycholic acid, may be of value in patients with jejunoileostomy.[44]

Although gastric bypass or gastroplasty may have less potential for gallstone formation than jejunoileostomy, it seems likely that some increased hazard will exist. These are, after all, obese patients undergoing weight loss (and cholesterol mobilization). If this is so, chenodeoxycholic or ursodeoxycholic acid therapy may be very reasonable in such patients.

In either situation, prophylaxis may not need to be carried out indefinitely, for Bennion and Grundy[6] have reported that after effective weight loss, cholesterol saturation in bile falls to normal. If so, in operated patients the need for bile acid therapy would be reduced or eliminated when the weight approaches near normal levels.

SUMMARY

An attempt has been made to identify the causes of increased cholesterol gallstone formation in obese patients both before and following jejunoileostomy. The prime lithogenic mechanism in obesity seems to be increased cholesterol mobilization and excretion in the bile. In jejunoileal bypass, a host of factors, including possibly limited bile salt synthesis, increased bile salt loss, and bacterial alteration of bile acids, along with the effects of rapid weight loss, may play a role. The identification and understanding of these factors will be important if attempts at prevention by administration of antibiotics to reduce bacterial overgrowth, or by giving chenodeoxycholic or ursodeoxycholic acid to replenish the diminished bile acid pools, are to be carried out.

REFERENCES

1. Admirand, W. H., and Small, D. M.: The physiochemical basis of cholesterol gallstone formation in man. J. Clin. Invest., *47*:1043, 1968.
2. Barber, J. C., Hayden, W. F., and Thompson, B. W.: Intestinal by-pass operations of obesity. Am. J. Surg., *126*:769, 1973.
3. Barry, R. E., Barisch, J., Bray, G. A., et al.: Intestinal adaptation after jejunoileal by-pass in man. Am. J. Clin. Nutr., *30*:32, 1977.
4. Been, J. M., Bills, P. M., and Lewis, D.: Microstruction of gallstones. Gastroenterology, 76:548, 1979.
5. Bell, C. C., Vlahcevic, Z. R., Prazich, J., et al.: Evidence that a diminshed bile acid pool precedes the formation of cholesterol gallstones in man. Surg. Gynecol. Obstet., *136*:961, 1973.
6. Bennion, L. J., and Grundy, S. M.: Effects of obesity and caloric intake on biliary lipid metabolism in man. J. Clin. Invest., *56*:996, 1975.
7. Bennion, L. J., and Grundy, S. M.: Risk factors for the development of cholelithiasis. New Engl. J. Med., *299*:1161; and *299*:22, 1221, 1978.
8. Cooper, J., Geizerora, H., and Oliver, M. F.: Clofibrate and gallstones. Lancet, *1*:1083, 1975.

9. The Coronary Drug Project Research Group: Gallbladder disease as a side effect of drugs influencing lipid metabolism. New Engl. J. Med., *296*:19, 1185, 1977.
10. Coyne, M. J., Marks, J., and Schoenfield, L. J.: Mechanism of cholesterol gallstone formation. Clin. Gastroenterol., *6*:129, 1977.
11. Dano, P., Lenz, K., and Justesen, T.: Bile acid metabolism and intestinal bacterial flora after three types of intestinal shunt operation. Scand. J. Gastroenterol., *9*:767, 1974.
12. DeWind, L. T., and Payne, J. H.: Intestinal by-pass surgery for morbid obesity. J.A.M.A., 236:20, 2298, 1976.
13. Evans, D. F., and Cussler, E. L.: Physiochemical considerations in gallstone pathogenesis. Hosp. Pract., *9*:133, 1974.
14. Faloon, W. W.: Ileal by-pass for obesity: Post-operative perspective. Hosp. Pract., *12*:73, 1977.
15. Faloon, W. W., Flood, M. S., Wilson, H., et al.: Gallstone formation and sterol changes in serum, bile and feces after jejunoileostomy for obesity (abstract). Gastroenterology, 76:1279, 1979.
16. Faloon, W. W., Rubulis, A., Knipp, J., et al.: Fecal fat, bile acid, and sterol excretion and biliary lipid changes in jejunoileostomy patients. Am. J. Clin. Nutr., *30*:21, 1977.
17. Friedman, G. D., Kannel, W. B., and Dawber, T. R.: The epidemiology of gallbladder disease: Observations in the Framingham study. J. Chron. Dis., *19*:273, 1966.
18. Gourlay, R. H., and Reynolds, C.: Complications of surgery for morbid obesity. Am. J. Surg., *126*:54, 1978.
19. Grundy, S. M.: Cholesterol-bile acid interactions in gallstone pathogenesis. Hosp. Pract., *8*:57, 1973.
20. Grundy, S. M.: Cholesterol metabolism in man. West. J. Med., *128*:13, 1978.
21. Grundy, S. M., Ahrens, E. H., Salen, G., et al.: Mechanisms of action of clofibrate on cholesterol metabolism in patients with hyperlipidemia. J. Lipid Res., *13*:531, 1972.
22. Grundy, S. M., Duane, W. C., Adler, R. D., et al.: Biliary lipid output in young women with cholesterol gallstones. Metabolism, 23:67–73, 1974.
23. Hardison, W. G. M., Tomaszewski, N., and Grundy, S. M.: Effect of acute alterations in small bowel transit time upon biliary excretion rate of bile acids. Gastroenterology, 76:568, 1979.
24. Heaton, K. D.: Disturbances of bile acid metabolism in intestinal disease. Clin. Gastroenterol., 6:69, 1977.
25. Holzbach, R. T., Marsh, M., Olszewski, M., et al.: Cholesterol solubility in bile. Evidence that supersaturated bile is frequent in healthy man. J. Clin. Invest., 52:1467, 1973.
26. Iser, J. H., Maton, P. N., Murphy, G. M., et al: Resistance to chenodeoxycholic acid (CDCA) treatment in obese patients with gallstones. Brit. Med. J., *1*:1509, 1978.
27. Kaye, M. D., and Kern, F.: Clinical relationships of gallstones. Lancet, *1*:1228, 1971.
28. Knecht, B. H.: Experience with gastric by-pass for massive obesity. Ann. Surg., *44*:496, 1978.
29. Lieber, M. M.: The incidence of gallstones and their correlation with other diseases. Ann. Surg., *135*:394, 1952.
30. Mabee, M., Meyer, P., Den Besten, L., et al.: The mechanism of increased gallstone formation in obese human subjects. Surgery, 79:460, 1976.
31. Madura, J. A., Loomis, R. C., Harris, R. A., et al.: Relationship of obesity to bile lithogenicity in man. Ann. Surg., *189*:106, 1979.
32. Metzger, A. L., Adler, R., Hemysfield, S., et al.: Lithogenic index—A numerical expression for the relative lithogenicity of bile. Gastroenterology, 62:499, 1972.
33. Miettinen, T. A.: Cholesterol production in obesity. Circulation, *44*:842, 1971.
34. Mok, H. Y. I., Von Bergman, K., Crouse, J. R., et al.: Biliary lipid metabolism in obesity: Effects of bile acid feeding before and during weight reduction. Gastroenterology, 76:556, 1979.
35. Salen, G., Nicolau, G., and Shefer, S., et al.: Hepatic cholesterol metabolism in patients with gallstones. Gastroenterology, 69:676, 1975.
36. Sampliner, R. E., Bennett, P. H., Comess, L. J., et al.: Gallbladder disease in Pima Indians. Demonstration of high prevalence and early onset by cholecystography. New Engl. J. Med., 283:1358, 1970.
37. Sarles, H., Crotle, C., Gerolami, A., et al.: The influence of caloric intake and of dietary protein on the bile lipids. Scand. J. Gastroenterol., 6:189, 1971.
38. Sarles, H., Hauton, J., Panche, E., et al.: Diet, cholesterol gallstones and composition of bile. Am. J. Dig. Dis., *15*:251, 1970.
39. Schaffer, E. A., and Small, D. M.: Biliary lipid secretion in cholesterol gallstone disease. The effect of cholecystectomy and obesity. J. Clin. Invest., 59:828, 1977.
40. Scott, H. W., Dean, R. H., Shull, H. J., et al.: Results of jejunoileal by-pass in two hundred patients with morbid obesity. Surg. Gynecol. Obstet., *145*:661, 1977.
41. Small, D. M., and Rapo, S.: Source of abnormal bile in patients with cholesterol gallstones. New Engl. J. Med., 283:2, 53, 1970.

42. Sorenson, I. A., Burnsgaard, A., Pederson, R., et al.: Lithogenic index of bile after jejunoileal by-pass operation of obesity. Scand. J. Gastroenterol. *12*:449, 1977.
43. Stein, L., and Wise, T.: Bile salt metabolism following jejunoileal by-pass for morbid obesity. Ann. Surg., *185*:67, 1977.
44. Stiebl, A., Czygan, P., Kommerell, B., et al.: Ursodeoxycholic acid versus chenodeoxycholic acid, comparison of their effects on bile acid and bile lipid composition in patients with cholesterol gallstones. Gastroenterology, 75:1016, 1978.
45. Telmos, A. H.: Long term morbidity of jejunoileal by-pass. Am. Surgeon, *43*:389, 1977.
46. Tyor, M. P.: Bile salt metabolism and the ileum. Viewpoints on Digestive Diseases, 2:1–4, 1976.
47. Vlahcevic, A. R., Bell, C. C., Buhac, F., et al.: Diminished bile acid pool size in patients with gallstones. Gastroenterology, *59*:165, 1970.
48. Wise, L., and Stein, T.: Biliary and urinary calculi: Pathogenesis following small bowel by-pass for obesity. Arch. Surg., *110*:1043, 1975.
49. Wise, L., and Stein, T.: Effect of jejuno-ileal by-pass on bile composition and formation of biliary calculi. Am. Surgeon, *187*:57, 1978.
50. Wood, P. D., Shioda, R., Estrick, D. L., et al.: Effect of cholestyramine on composition of duodenal bile in obese human subjects. Metabolism, *21*:107, 1972.

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Gastric Bypass for Morbid Obesity

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As experience with the long-term management of patients suffering from morbid obesity grows, a number of facts emerge. Morbid obesity in itself will decrease life expectancy. It is also associated with the early development of cardiopulmonary disorders, hypertension, and diabetes as well as a more accelerated course of these diseases. The nonoperative management of morbid obesity rarely leads to permanent weight reduction and, in fact, is often associated with intermittent increases and decreases in weight which may be more detrimental to health than maintaining the state of morbid obesity.

While a variety of operative procedures have been recommended for the production of permanent weight loss in patients with morbid obesity, only two have withstood the test of time: the jejunoileal bypass operation, with its rationale of increasing caloric loss in the feces, and the gastric bypass procedure, with its rationale of decreasing caloric intake. This article will deal with the gastric bypass operations in distinction to the newer, and as yet incompletely tested, gastroplastic procedures. The gastric bypass operation is an exclusion procedure which was developed by Dr. Edward Mason of the University of Iowa in 1966.[9] It produces weight loss by restricting caloric intake without interfering appreciably with the absorptive capacity of the bowel. Thus the adverse metabolic and nutritional effects of the small bowel bypass procedures are avoided. Three gastric bypass procedures will be described after which the surgical complications, metabolic complications, advantages and disadvantages of these operations will be discussed.

SELECTION OF PATIENTS

The single most important criterion for consideration of an operative procedure for obesity is that the patient be morbidly obese. Morbid obesity has been variously defined by a number of authors reporting on the gastric bypass procedure, but the definitions are based on an absolute weight (50

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kg or 100 pounds over ideal body weight), or a relative definition of body weight (more than twice the ideal weight). While "ideal weight" itself has been obtained from tables provided by insurance statistics, Devine[4] has developed a formula for determining ideal weight which can be applied to all individuals and takes into account differences in weight according to sex: For females, ideal body = 45 kg + 2.3 kg per inch over 5 feet in height; and for males, ideal body weight = 50 kg + 2.3 kg per inch over 5 feet. Most investigators also insist that their patients have participated in a weight control program and have shown some decrease in weight while on the program. Concomitant diseases are frequent and, of themselves, do not constitute a contraindication to the gastric bypass operation. In fact, some of these ailments, such as hypertension, diabetes, narcolepsy, and arthritis, are often improved by the weight loss resulting from the operation.

Psychiatric evaluation of candidates for the operation has gone almost full circle. Since it is recognized that patients with morbid obesity suffer from some psychological problem, psychiatric screening was an essential part of the evaluation. This was felt to be particularly important for the gastric bypass operation since overeating seemed to be the mechanism whereby these individuals cope with stressful situations, and one of the assured effects of the gastric bypass operation was the inability to eat great quantities of food. However, with experience, the involvement of the psychiatrist in the screening of these patients preoperatively has dwindled. In our institution this has been a mutual decision because it has become apparent that it is not possible to predict a patient's psychological reaction to the operation even with the use of extensive psychological testing. While the operation will not reverse severe psychiatric illness, it only rarely worsens the situation.

OPERATIVE PROCEDURES

The concept of the gastric bypass procedure was based on the observation that patients with peptic ulcer disease who underwent 75 to 80 per cent subtotal gastric resection often had difficulty maintaining weight. Several features are common to all the gastric bypass procedures:

1. The distal stomach is not resected, so that the operation is reversible if necessary.

2. The amount of stomach remaining in continuity with the rest of the gastrointestinal tract represents about 10 per cent of the stomach and perhaps is best measured by a standard volume determination as suggested by Alder and Terry.[2] A suggested volume of 50 dl capacity appears to be appropriate.

3. The anastomosis between the stomach and the jejunum is made no greater than 12 mm in diameter.

Thus, the basic principles of the gastric bypass procedure are rapid filling and slow emptying which produce a prolonged feeling of satiety.

The gastric bypass originally described by Mason and Ito[9] involves a transection of the stomach so that the upper segment has a volume of approximately 60 dl. The distal cut end of the stomach is oversewn completely with Lembert sutures. The proximal cut end of the stomach is

Figure 1. The gastric bypass originally described by Mason and Ito involved transection of the stomach. See text for details. (*From* Mason, E. E., and Ito, C.: Gastric bypass. Ann. Surg., *170*:329, 1969, with permission.)

oversewn from the lesser curve side to within 1.2 cm of the greater curve. A loop of jejunum is then brought up to this small opening through the transverse mesocolon and an end-to-side gastrojejunostomy performed. The stomach is then brought down and attached to the opening in the transverse mesocolon to prevent both internal hernia and twisting of the jejunal loop (Fig. 1).

In 1977 Alden[1] described a different technique of gastric bypass in which he did not transect the stomach. Instead a complete staple line is placed across the stomach, again dividing it into a proximal segment with a volume of approximately 60 dl and a much larger distal segment. The jejunum is then brought up in antecolic fashion, and a 1.2 cm side-to-side stapled anastomosis is made between the greater curvature of the stomach and the jejunum. This procedure avoids a transection of the stomach and its possible effect in interfering further with the blood supply at the anastomotic site, and also can be performed relatively quickly (Fig. 2).

Between 1974 and 1977 we conducted a comparative study of the gastric bypass and jejunoileal bypass for morbid obesity.[5] At the beginning of that study the technique of Mason was used. However, bringing the stomach down below the transverse mesocolon seemed both difficult and hazardous. Thus, a Roux-en-Y type of reconstitution was used. In that study the majority of the patients who underwent gastric bypass had transection of the stomach as described by Mason, after which the

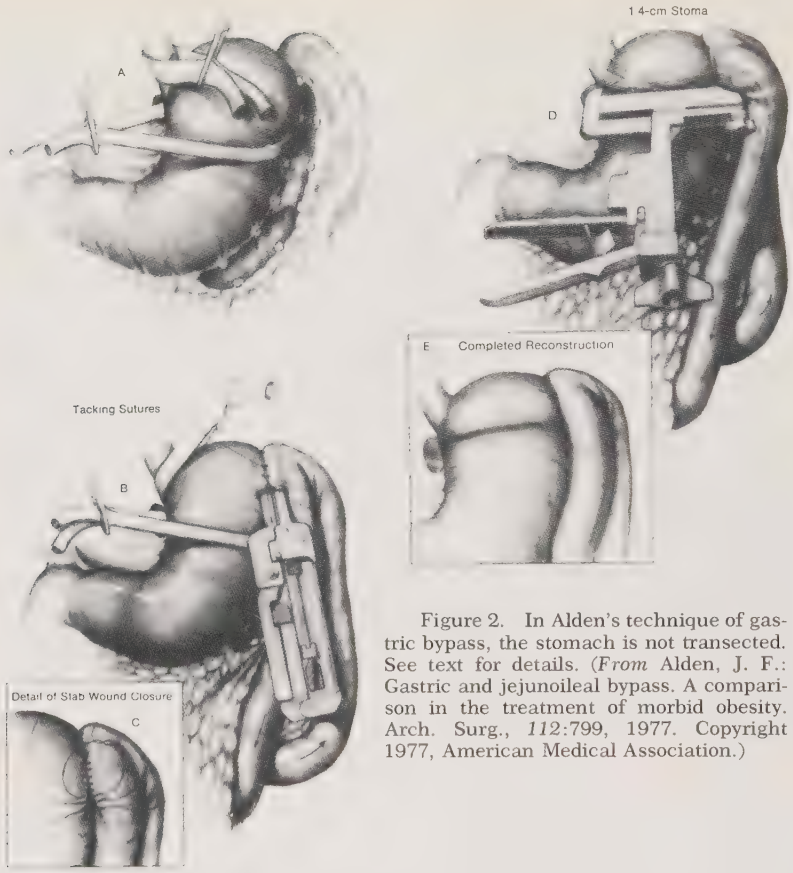

Figure 2. In Alden's technique of gastric bypass, the stomach is not transected. See text for details. (*From* Alden, J. F.: Gastric and jejunoileal bypass. A comparison in the treatment of morbid obesity. Arch. Surg., *112*:799, 1977. Copyright 1977, American Medical Association.)

jejunum was transected with a stapler 12 to 15 cm beyond the ligament of Treitz. The distal cut end of the jejunum was then oversewn with interrupted 3-0 seromuscular sutures and brought through an opening in the transverse mesocolon, behind the distal stomach, and up to the cut edge of the proximal gastric pouch. This edge was then oversewn with interrupted 3-0 seromuscular sutures down to a point 1.2 cm from the greater curvature and an end-to-side anastomosis then made between the stomach and the retrocolic jejunal limb. The limb was then tacked circumferentially to the opening in the mesocolon and an end-to-side jejunojejunostomy was constructed 35 cm distal to the gastrojejunostomy (Fig. 3). More recently, this author has not transected the stomach but has simply placed a complete staple line across it similar to Alden's technique, but continues to use the Roux-en-Y anastomosis, making a side-to-side gastrojejunostomy on the greater curvature side of the stomach 2 cm distal to the gastroesophageal junction.

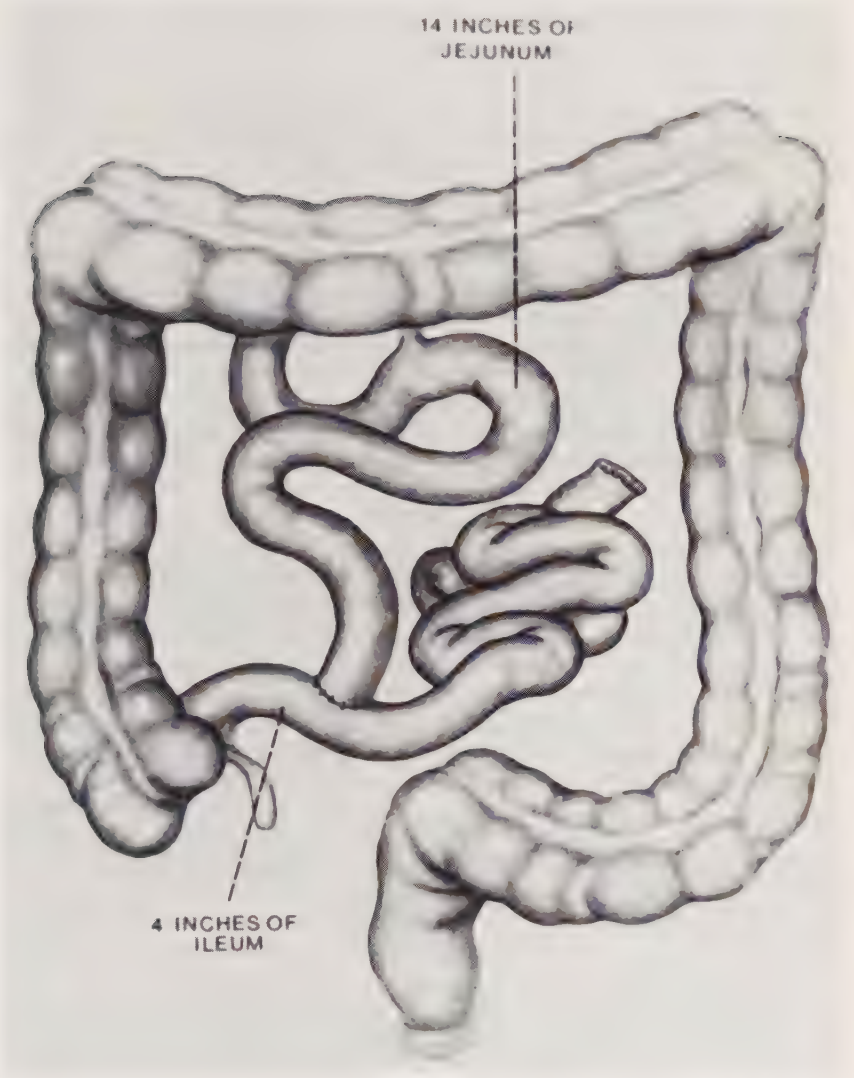

Figure 3. See text for details. (*From* Griffen, W. O., Jr., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. Ann. Surg., *186*:500, 1977, with permission.)

REPORTED RESULTS

At a recent workshop, a total of 1585 patients were reported as having undergone gastric bypass.[3, 6, 7, 8, 11, 12] The weight loss following the gastric bypass procedures has been quite satisfactory in the majority of cases and in the two comparative studies,[3, 5] as good as the weight loss seen after jejunoileal bypass. Dr. Mason's original paper described satisfactory weight loss in 75 per cent of the patients, with a less than satisfactory weight loss in 25 per cent. In the total number of patients now reported to have undergone gastric bypass for morbid obesity, inadequate weight loss at the outset occurs in approximately 8 per cent.

It is possible to overeat the pouch if the individual consumes foods of low volume and high caloric content. There are two types of patients with morbid obesity, the "snackers" and the "gorgers." The former group are more likely to be able to overeat the pouch than the latter. In general, the individuals who gorge themselves simply change their eating habits following the gastric bypass operation and do quite satisfactorily. On the other hand, unless the "snackers" watch their intake carefully, their weight reduction can be unsatisfactory. The average weight reduction reported in the total population of these series is 47.6 kg in one year. In no instance has excessive weight loss to a point below ideal body weight been reported following gastric bypass.

The postoperative mortality in the 1585 patients is 1.6 per cent. Early complications include anastomotic leak, pulmonary embolism, wound infections, urinary tract infections, and other less common difficulties. The overall early complication rate is 22 per cent. Late complications include failure to lose weight satisfactorily (8 per cent), ventral hernia, persistent vomiting, hair loss, marginal ulcer, and other less common cited problems. The overall late complication rate is 17 per cent.

Patient satisfaction is high, with 90 per cent of the patients showing no untoward effects or only minor problems such as occasional vomiting when they overeat. In patients followed for more than five years, late weight gain has occurred in less than 5 per cent. The psychological response to the operation, and its capability of producing a permanent weight reduction, has been positive in the majority of patients.

COMMENTS

Certain features of the gastric bypass operation deserve special attention. First, almost all surgeons who have performed the gastric bypass operation for morbid obesity have found that there is a definite learning curve in the procedure. The first patient in our own series lost less than 10 per cent of his body weight in the first six months following the operation. The meal capacity reported by this patient within three months of the operation clearly indicated that the remaining pouch was entirely too large. The pouch must be small, and while recommendations now are that the pouch be measured at a volume of 60 dl, the tendency is to make the pouch smaller than that because of the occasional patient who does not lose a sufficient amount of weight.

The size of the anastomosis between the stomach and jejunum is also critical. Whether a loop jejunostomy or a Roux-en-Y reconstitution is used, a large anastomosis provides the pouch with an easy and sizable outflow, which permits the individual to consume more calories and thus lose an insufficient amount of weight. Thus, the entire concept of the gastric bypass operation is to provide a receptacle for food which is quite small and empties slowly. When these two features are properly met, the patients often comment on the fact that they feel full early after a meal and that the satiety lasts for a considerable period of time.

Late weight gain has not been a particularly noticeable problem. Although during the first postoperative year, the patients do find that they can eat a greater quantity of food, they still become uncomfortable if they eat too much or too rapidly. Therefore, they continue to lose weight throughout the year, although at a slower rate than in the immediate postoperative period. Almost invariably, the 5 per cent of the patients who put on a considerable amount of weight after losing satisfactorily are those who have stretched a pouch, which was probably too large initially, and those who tend to snack rather than eat three meals a day. Inadequate weight loss, or regaining a large amount of weight, can be treated by revision of the gastric pouch, revision of the gastrojejunostomy, or both. This has produced good results as a secondary procedure and is preferred by the author to the addition of a jejunoileal bypass following a gastric bypass operation.

Mini-dose heparin as a means of lessening deep vein thrombosis and preventing a postoperative pulmonary embolus seems to be a matter of the surgeon's choice. Printen[11] has indicated that these patients are at no greater risk to thromboembolic disease than the normal population, but many surgeons continue to use mini-dose heparin without experiencing any untoward effect in the intraoperative or postoperative period. It is also feasible to perform other procedures during the gastric bypass operation and such operations as cholecystectomy, tubal ligation, ventral and umbilical hernia repair, ovarian cystectomy, and even inferior vena caval interruption have been reported as accompanying procedures.

There is no question that an anastomotic leak is the most serious complication of the gastric bypass procedure, the incidence being reported to be 4.4 per cent. It is the complication which is most likely to lead to a postoperative death, and that usually because of a delay in making the diagnosis. A temperature elevation of greater than 30.8° C (102° F) and, more importantly, a pulse rate of greater than 130 beats per minute in the early postoperative period, should make one suspicious of an anastomotic leak. It is then necessary to obtain a Gastrografin swallow in order to confirm such a leak and to proceed to the operating room for correction of the situation. Generally, the procedure needed for correction is identification of the leak and closure, adequate drainage of the left subphrenic space, and provision of a means of enteral nutrition for future use.

There are several advantages of the Roux-en-Y anastomosis in patients in whom an anastomotic leak develops following gastric bypass. First, the material which goes into the left subphrenic space rarely contains bile or pancreatic juice, nor does a continuing leak contain such material. As far as can be ascertained, a leak occurring in a patient who

has had a Roux-en-Y anastomosis has not resulted in a postoperative death; whereas leaks occurring following a loop gastrojejunostomy have. Second, the provision of a pathway for enteral nutrition following the closure of the leak can be accomplished simply by placing a standard gastrostomy into the distal bypassed stomach. Once peristalsis begins, feeding through the gastrostomy can be done and the need for a central venous line and its attendant complications can be avoided.

In several long-term follow-up studies the incidence of nephrolithiasis following gastric bypass has been considerably less than that seen with jejunoileal bypass. While the mechanism of oxaluria and stone formation in patients with ileal dysfunction is not completely understood, it is apparent that high dietary oxalate and dietary fat malabsorption will increase urinary oxalate excretion considerably. Since ileal dysfunction is not seen in patients with gastric bypass, oxalate stone formation should be lower in patients following the gastric procedure. An additional factor may be one of dehydration which is not commonly recognized in gastric bypass patients, as compared to jejunoileal bypass patients. Thus, the incidence of stone formation following gastric bypass is of the magnitude of 1 per cent as compared to about 10 per cent in the jejunoileal group. An interesting feature of the nephrolithiasis seen after gastric bypass procedures is the high incidence of uric acid stones in these patients.

There have been no reported instances of liver disease following gastric bypass operations. In the prospective study previously mentioned, serial liver biopsies were performed on patients undergoing gastric bypass. Almost invariably the liver biopsies done at the time of the bypass procedure showed fatty infiltration and occasionally some periportal inflammatory reaction. Percutaneous liver biopsies done one year following the procedure showed improvement in the histologic picture of the liver in 75 per cent of the cases and no change in the remainder. There were no instances in which the histologic pattern had worsened after the operation. In a few instances, the liver biopsy done one year postoperatively was actually interpreted by the pathologist, who knew nothing about the clinical history, as being a normal liver. This finding is undoubtedly related to the fact that the gastric bypass procedure is one which simply reduces caloric intake without interfering with absorptive processes.

The psychological response to the operation has been quite gratifying. At first consideration of the operation, psychiatrists were concerned about the removal of the patient's coping mechanism and what effect it might have on patients who are psychologically impaired. Moreover, some surgeons contend that patients undergoing gastric bypass procedures are "food gorgers" and that patients have complained bitterly in the postoperative period about being unable to ingest a large quantity of food.[13] In the reports on gastric bypass, as well as my own personal experience, that has been a minor difficulty. Once the patients have learned the proper method of eating, they fill the gastric pouch quickly, with a resultant feeling of satiety that only disappears slowly as the pouch empties. In fact, many patients expressed their great pleasure at being able to detect a weight loss on a weekly basis. In other words, for those patients who have consented to undergo the drastic step of having an operation to control their weight, loss of weight has become the primary motivating force in

their lives. Thus it is not surprising that the psychological response to the operation is good, although it should be emphasized again that the operation is not designed to *treat* the psychological impairment of the individual.

Several contraindications to the gastric bypass procedure have been suggested in the literature. Obviously, the patient must be a good operative risk in order to undergo such a major procedure. While Printen et al.[10] have published results on the gastric bypass procedure in patients over the age of 50 and indicated that this group does not respond as well as younger patients, age per se is not a contraindication to a gastric bypass procedure. Many older patients operated upon are suffering from severe disabling arthritis and some are even confined to a wheelchair because of an arthritic condition. Such patients do well even though their weight loss may not be as good as that seen with younger individuals. Eliminating the necessity for the weight-bearing joints to carry an additional 20 to 30 kg can remarkably ameliorate these symptoms.

Duodenal ulcer disease and hiatal hernia have both been considered to be contraindications to the gastric bypass procedure.[7] Active ulcer disease probably is a contraindication, but patients who give a history of having had a duodenal ulcer in the past have undergone gastric bypass surgery without recognizable difficulty. While some authors have advocated performing a vagotomy and pyloroplasty in these patients at the time of gastric bypass surgery, others have simply performed the gastric bypass without vagotomy and have not reported any untoward effects. Marginal ulcer disease, which was commented upon when Mason presented the first report of gastric bypass, has not proved to be a serious postoperative problem, even in those patients undergoing a Roux-en-Y anastomosis. This is probably because the gastric pouch contains few parietal cells and cannot produce much hydrochloric acid. Hiatal hernia with reflux esophagitis is not a contraindication if a Roux-en-Y anastomosis is used. A loop gastrojejunostomy so close to the gastroesophageal junction may result in bile esophagitis if a hiatal hernia is present. However, the Roux-en-Y anastomosis eliminates bile reflux into the gastric pouch and has been done without any anti-reflux procedure in symptomatic patients with amelioration of the reflux esophagitis in all but a few patients and the disappearance of demonstrable esophagitis by endoscopy in all patients.

The gastric bypass operation is an excellent procedure for a patient who has had a jejunoileal bypass and requires a takedown of the small bowel bypass because of untoward metabolic effects. It is well recognized that if the jejunoileal bypass is simply taken down and the patient's small bowel reconstituted, weight gain is inevitable and the patient will once again become morbidly obese. Therefore, it is necessary to provide these individuals with a means of maintaining weight reduction. Addition of more small bowel into the nutrient stream has not proved successful. On the other hand, Taper et al.[14] have reported excellent results in four patients with conversion to gastric bypass, and this author has now had experience with 20 patients with most satisfactory results. The conversion of the jejunoileal bypass to a Roux-en-Y gastric bypass is an operation that can be accomplished in two hours and has been done with no

mortality and minimal morbidity. Patient satisfaction with the conversion operation has been high.

SUMMARY

The gastric bypass operation is designed to decrease the size of the food receptacle so that a limited number of calories can be ingested. All food ingested is absorbed normally, thus eliminating problems that may be associated with metabolic derangements. Although it is possible to overeat the gastric pouch, the overall result of gastric bypass, in terms of weight loss, is quite satisfactory, and the mortality rate of less than 2 per cent and the morbidity rate of less than 20 per cent are also acceptable. Late complications following gastric bypass are low: specifically, nephrolithiasis is eight to 10 times less frequent than after jejunoileal bypass. Liver disease has not been seen following gastric bypass.

REFERENCES

1. Alden, J. F.: Gastric and jejunoileal bypass. A comparison in the treatment of morbid obesity. Arch. Surg., *112*:799, 1977.
2. Alder, R. L., and Terry, B. E.: Measurement and standardization of the gastric pouch in gastric bypass. Surg. Gynecol. Obstet., *144*:762, 1977.
3. Buckwalter, J. A.: A prospective comparison of the jejunoileal and gastric bypass operations for morbid obesity. World J. Surg., *1*:757, 1977.
4. Devine, B. J.: Gentamicine therapy. Drug Intell. Clin. Pharm. *8*:650, 1974.
5. Griffen, W. O., Jr., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. Ann. Surg., *186*:500, 1977.
6. Griffen, W. O., Jr.: Personal data.
7. Hermreck, A. S., Jewell, W. R., and Hardin, C. A.: Gastric bypass for morbid obesity: Results and complications. Surgery, *80*:498, 1976.
8. Knecht, B. H.: Experience with gastric bypass for massive obesity. Am. Surgeon, *44*:496, 1978.
9. Mason, E. E., and Ito, C.: Gastric bypass. Ann. Surg., *170*:329, 1969.
10. Printen, K. J., and Mason, E. E.: Gastric bypass for morbid obesity in patients more than fifty years of age. Surg. Gynecol. Obstet., *144*:192, 1977.
11. Printen, K. J., Miller, E. V., Mason, E. E., et al.: Venous thromboembolism in the morbidly obese. Surg. Gynecol. Obstet., *147*:63, 1978.
12. Seay, J. E., III: Personal communication.
13. Stephenson, S. E., Jr.: Clinical trial of surgery for morbid obesity. Editorial comment. South. Med. J., *71*:1370, 1978.
14. Tapper, D., Hunt, T. K., Allen, R. C., et al.: Conversion of jejunoileal bypass to gastric bypass to maintain weight loss. Surg. Gynecol. Obstet., *147*:353, 1978.

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Gastroplasty in Morbid Obesity

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The past 25 years have seen several approaches to the problem of morbid obesity. Kremen, Linner, and Nelson[10] designed the first jejunoileal bypass and reported on an experimental 90 per cent end-to-end jejunoileal bypass in dogs. Payne, DeWind, and Commons[14] reported on the clinical study of 10 patients undergoing jejunocolic and jejunoileal shunts. Payne and DeWind[15] introduced the 14-4 end-to-side jejunoileal bypass. This was followed in 1973[16] and 1976[6] by reports of long-term results of a larger series of patients by the same authors. Scott and associates[18] modified the procedure in 1971, converting it to the end-to-end jejunoileal bypass; in 1973 they reported on their first 72 patients, followed by a larger series of 200 cases reported in 1977.[20] In 1975 Buchwald and associates[3] published an excellent clinical monogram on intestinal bypass procedures.

Mason and Ito[11] introduced the gastric bypass operation in 1967, and in 1973, Printen and Mason[17] reported on their experience with 130 gastric bypasses and 56 gastroplasties. They observed that the gastroplasty fundic pouch enlarged, and the diameter of the channel increased, contributing to a failure to achieve adequate weight loss. These results were later improved upon by the use of a smaller pouch and opening.[5, 12] The results and complications of gastric bypass were reported,[9] and comparative studies of gastric bypass and jejunoileal bypass procedures were published,[1, 4, 8] the authors expressing their preference for the gastric bypass.

More recently, this author[7] introduced a modified gastroplasty procedure consisting of a 60 ml fundic reservoir and a 12 mm channel located on the greater curvature of the stomach. A total of 330 patients were divided into three groups: Group I (173 patients) with no support to the channel; Group II (30 patients) with external support using a narrow strip of Dacron mesh around the channel; and Group III (127 patients) with an internal seromuscular suture ring. Expansion of the unsupported channel concurred with the previous observations of Printen and Mason. Significant stenosis of the channel developed in Group II patients, and the author warned against the use of synthetic mesh for this purpose. Although Group III patients had been followed for only six months, statisti-

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cally significant advantages were seen in this group, especially in reference to weight loss.

The purpose of this presentation is to report on a group of patients who were subjected to gastroplasty surgery using the seromuscular suture support technique and to include a 12-month follow-up study.

MATERIALS AND METHODS

The series consists of 200 patients. The mean age was 34.2 years, with a range of 14 to 61 years. Females predominated, 154 to 46. The mean number of kg overweight was 67.4, with a range of 45.5 to 146.4 kg. Basic guidelines for selection of patients consisted of: excess weight of at least 45.5 kg; obesity for at least five years; patient free of severe metabolic or endocrine problems; neuropsychiatric consultations for patients with mental disturbances in their medical history; documentation of trial at weight reduction by acceptable medical criteria; and willingness to participate in the long-term follow-up protocol. In lengthy initial interview, all aspects of the procedure, including mortality and morbidity, were discussed. Upon admission to the hospital, the patient received an illustrated gastroplasty manual, outlining in detail all aspects of the medical work-up. Patients undergo metabolic, gastrointestinal, pulmonary, cardiac, and renal studies.

Gastroplasty classes in nutrition are conducted prior to surgery by the dietitians of the department of clinical nutrition. These sessions are designed to assist patients in making the proper psychological adaptation to the new life-style imposed, with special reference to dietary habits and restrictions. Food trays are displayed in order to give patients a realistic picture of the gastric capacity after surgery. The classes stress the importance of adequate protein and fluid replacement and the various ways they can be achieved. The necessity for eating slowly and meticulous mastication is emphasized. Patients are warned of the resultant consequences when basic guidelines are not followed.

This learning process has contributed to the patient's confidence and reassurance, and has served as an effective screening process. Unsure patients may change their minds when this preparative information has been made known to them.

OPERATIVE TECHNIQUE

A midline incision is employed from the xyphoid process to the umbilicus. The gastroplasty retractor adds safety and operator comfort. The operating table is placed in the reversed Trendelenberg position with a foot-plate support. This position enhances the patient's ventilatory exchange and improves exposure of the upper abdomen as the viscera migrate to the pelvis. Intermittent pulsatile venous boots are used to prevent venous stasis resulting from such dependency. Heparin, 5000 units, is given subcutaneously, three hours before surgery, and low dose heparinization is carried through the fifth postoperative day.

The fundus of the stomach is mobilized, starting at the esophagus and carried distally to include only the first two or three vasa brevia to the spleen. Further distal dissection is seldom necessary. A small opening is made in the lesser curvature, distal to the superior branches of the left gastric artery and close to the serosal surface of the stomach, avoiding the neurovascular structures (Fig. 1). The C-clamp attachment for the T.A. 90 stapler aligns the staples, avoiding the gastric perforation when the guide pin is used (Fig. 2). The T.A. 90 stapler is inserted from the lesser toward the greater curvature of the stomach, against a 7 mm Maloney esophageal bougie (Fig. 3). Since the distance between the last staple and the end of the cartridge measures 7 mm, the channel formed measures 14 mm in diameter. Two staples are used, placed as close to each other as possible. The 7 mm bougie is removed and a 12 mm Maloney bougie is inserted (Fig. 4). The seromuscular suture ring, using 2-0 polypropylene, starts at the end of the staple line, transfixing the last three or four staples. Presently, an O chromic catgut suture is tied around the channel to facilitate the insertion of the polypropylene suture, as recommended by Mason.[13] The seromuscular imbricating suture is brought from the posterior to the anterior gastric wall around the channel and against the bougie; it is then brought back around to the starting point (Fig. 5). A second layer of interrupted Dacron sutures is inserted in the Lembert manner to cover the first suture line. A 12 mm channel is formed as the bougie is removed (Fig. 6). Sixty cc of saline distends the properly constructed pouch (Fig. 7). (Alder and Terry[2] made excellent recommendations on the measurement of size of the gastric pouch at the time of surgery.) The nasogastric tube is advanced through the channel to provide decompression of both proximal and distal segments.

The operating time is usually 60 minutes. Blood transfusions have not been necessary. Blood gases are serially determined as indicated. Patients are usually extubated immediately after surgery. Occasionally, assisted respiration is required in the recovery room; intensive care is seldom required. The nasogastric tube is removed, as a rule, on the second postoperative day. A liquid diet, consisting of tea, broth, gelatin and a liquid protein supplement, is given on the third postoperative day; strained soups and vegetables, milk, and sherbet on the fourth; and the gastroplasty bland diet is started on the fifth postoperative day. The total caloric intake is between 350 and 500 for the three meals. A gradual increase is expected to double that amount in 12 weeks.

RESULTS

The early postoperative complications included wound sepsis, 12; dehiscence, 1; acute perforation of the pouch, 2; subphrenic abscess, 2; pneumonia, 8; atelectasis, 10; urinary tract infection, 1; and 1 patient died of myocardial insufficiency with ventricular fibrillation. The total number of complications was 37, or 18.5 per cent. The etiology of the perforations is probably a combination of ischemia and hyperacidity of the pouch. Since fewer vessels have been ligated on the greater curvature and patients have been placed on intravenous cimetidine after surgery, no further perforations have occurred.

Figure 1

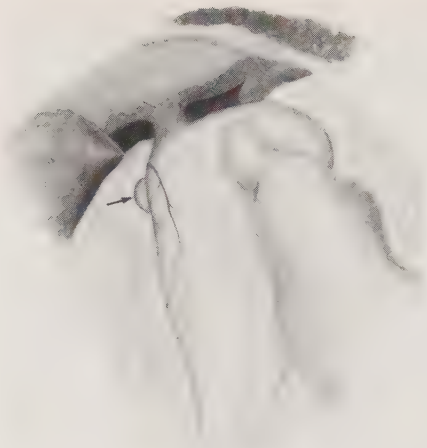

Figure 2

Figure 3

Figure 4

Figure 1. Mobilized fundus with fingertip visible distal to branch of left gastric artery near esophagogastric junction.

Figure 2. T. A. 90 stapler and C-clamp assembly.

Figure 3. T. A. 90 stapler with C-clamp assembly is used to apply the second row of staples.

Figure 4. Completed gastroplasty with 12 mm Maloney bougie through channel.

Figure 5

Figure 6 Figure 7

Figure 5. Seromuscular suture ring of 2-0 polypropylene.

Figure 6. Operative technique. Completed gastroplasty.

Figure 7. Fundic pouch distended with 60 cc of saline.

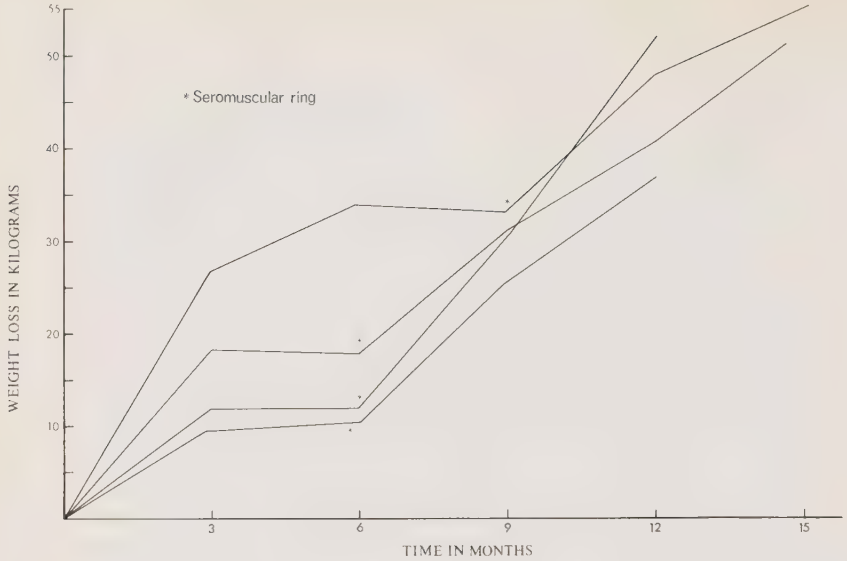

Figure 8. Four gastroplasty revisions with addition of the seromuscular ring for a 12 mm channel.

Late postoperative complications have been limited to vomiting, which occurred in 32 patients (16 per cent). Revisions were required for three staple-line disruptions, three cases of broken 3-0 polypropylene suture (2-0 polypropylene is now used), and three cases of stenosis of the channel, for a total of 4.5 per cent.

Table 1. *Mean Weight Loss After Gastroplasty*

TIME (MONTHS)	NO. OF PATIENTS	RANGE (KG)	MEAN (KG)	PER CENT DECREASE FROM PREOPERATIVE WEIGHT	PER CENT OF GOAL
3	180	8.2–39.5	18.6	16.9	34.5
6	137	13.6–50.0	29.0	22.9	49.8
9	92	17.7–78.6	35.9	30.7	67.6
12	47	18.6–88.2	39.8	34.1	77.9

Table 2. *Relationship Between Channel Diameter and Surface Area*

$A = \pi r^2$

$\pi 5^2 = 78.5^{mm^2} - 30\%$

$\pi 6^2 = 113^{mm^2}$ (12 mm channel)

$\pi 7^2 = 153.8^{mm^2} + 36\%$

$\pi 8^2 = 200.9^{mm^2} + 77\%$

Vomiting has been the main reason, other than revisions, for rehospitalization. One small sinus tract, discovered two weeks after surgery, was treated with nasogastric decompression, with no further complications. Wound sepsis, perforated pouch, pulmonary embolism, and subphrenic abscess, in one case each, necessitated rehospitalization, and with three other miscellaneous causes, accounted for a rehospitalization rate of 7 per cent for reasons other than revision.

Weight loss is expressed as mean weight loss, as per cent decrease from the preoperative weight, and as per cent of the goal (Table 1). The goal is determined as ideal weight plus 20 per cent. Four revisions (Fig. 8) indicate that weight loss is again initiated when the channel is back to 12 mm in diameter. Table 2 may help to explain weight loss failure when the unsupported channel increases its diameter.

SUMMARY AND CONCLUSIONS

Bariatric surgeons will continue to meet frequently to compare statistical data. No doubt new procedures will continue to evolve, and those now existing will be modified and refined. We need to learn not only from our successes but also from our failures.

The patient undergoing gastroplasty surgery has to make a significant psychological adaptation to the newly imposed dietary demands. He cannot do it alone. He needs the support of his family, the surgeon, the nursing staff, and the dietary department. It is imperative to provide a well organized, informative, and educational program for the patient, in which the team concept is most important. Careful screening of patients is essential, accompanied by proper postoperative evaluation. Failures need to be carefully studied to determine the factor, or factors, responsible. In most instances revision or re-education may convert the failure to a success.

From the technical standpoint, the operation is effective only when a small fundic reservoir is formed with a nonexpanding 12 mm channel. The seromuscular suture support to the channel appears to be a reasonable solution to this problem. Continued long-term follow-up is needed for further evaluation of the operation as it now stands. The size of the channel is technically critical and the prevention of channel enlargement the ultimate goal.

REFERENCES

1. Alden, J. F.: Gastric and jejuno-ileal bypass: A comparison in the treatment of morbid obesity. Arch. Surg., *112*:799, 1977.
2. Alder, R. L., and Terry, B. E.: Measurement of standardization of the gastric pouch in gastric bypass. Surg. Gynecol. Obstet., *144*:762, 1977.
3. Buchwald, H., Varco, R. L., Moore, R. B., et al.: Intestinal bypass procedures. Curr. Prob. Surg., April 1975, pp. 1-51.
4. Buckwalter, J. A.: A prospective comparison of the jejuno-ileal and gastric bypass operations for morbid obesity. World J. Surg., *1*:757, 1977.
5. Cohen, W. M., Mason, E. E., and Bloomers, T. J.: Gastric bypass for morbid obesity. Radiology, *122*:609, 1977.
6. DeWind, L. T., and Payne, J. H.: Intestinal bypass surgery for morbid obesity: Long term results. J.A.M.A., *236*:2298, 1976.

7. Gomez, C. A.: Gastroplasty in the surgical treatment of morbid obesity. Am. J. Clin. Nutr., in press.
8. Griffen, W. O., Jr., Young, V. L., and Stevenson, C. C.: A prospective comparison of gastric and jejunoileal bypass procedure for morbid obesity. Ann. Surg., *186*:500, 1977.
9. Hermeck, A. S., Jewel, W. R., and Hardin, C. A.: Gastric bypass for morbid obesity: Results and complications. Surgery, *80*:498, 1976.
10. Kremen, A. N., Linner, J. H., and Nelson, C. H.: Experimental evaluation of the nutritional importance of proximal and distal small intestine. Ann. Surg., *140*:439, 1954.
11. Mason, E. E., and Ito, C.: Gastric bypass in obesity. SURG. CLIN. NORTH AM., *47*:1345, 1967.
12. Mason, E. E., Printen, K. J., Hartford, C. E., et al.: Optimizing results of gastric bypass. Ann. Surg., *182*:405, 1975.
13. Mason, E. E.: Personal communication.
14. Payne, J. H.: Surgical treatment of obesity: Sixteen years experience. Arch. Surg., *106*:432, 1973.
15. Payne, J. H., and DeWind, L. T.: Surgical treatment of obesity. Am. J. Surg., *118*:141, 1969.
16. Payne, J. H., DeWind, L. T., and Commons, R. R.: Metabolic observations in patients with jejunoileal shunts. Am. J. Surg., *106*:273, 1963.
17. Printen, K. J., and Mason, E. E.: Gastric bypass for relief of morbid obesity. Arch. Surg., *106*:428, 1973.
18. Scott, H. W., Jr., Sandstead, H. H., Brill, A. B., et al.: Experience with a new technic of intestinal bypass in the treatment of morbid obesity. Ann. Surg., *174*:560, 1971.
19. Scott, H. W., Jr., Dean, R. H., Shull, H. J., et al: New considerations in use of jejunoileal bypass in patients with morbid obesity. Ann. Surg., *177*:723, 1973.
20. Scott, H. W., Jr., Dean, R. H., Shull, H. J., et al.: Results of jejuno-ileal bypass in 200 patients with morbid obesity. Surg. Gynecol. Obstet., *145*:661, 1977.

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Surgical Approaches for Failed Jejunoileal Bypass and Failed Gastric Bypass

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Today a great deal of controversy surrounds the field of bypass surgery for obesity. Some physicians condemn all bypass procedures; surgeons contend with other surgeons concerning the relative efficacy of jejunoileal bypass versus gastric bypass; and nearly every month someone publishes a "new" procedure, one that is usually a variant of a previous operation, but that promises dramatic results free of complications. In such a circus atmosphere, serious surgical efforts to provide productive and realistic alternatives in the therapy of this major disease problem can go unheeded and, indeed, be lost to the scientific community and to the patients whom we seek to serve. It must be remembered that all current surgical approaches to the management of morbid obesity are an approximation to rational therapy, since surgery attempts to alter either absorption or the capacity for intake of food and does not directly attack the cause of overeating.

Certain advantages and disadvantages are associated with each of the two common classes of procedures, and both jejunoileal and gastric bypass operations will require revision procedures or take-down under certain circumstances. With adequate preoperative preparation for surgery, and extended postoperative follow-up care, less than 5 per cent of bypass procedures should, however, require remedial operation.

JEJUNOILEAL BYPASS

Causes of Failure

Jejunoileal bypass has inevitable side effects and unique complications.

Side effects occur in all patients.[4, 5] Diarrhea is common, necessitating, in most patients, drug control for one year. At one year, 90 per cent of

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patients have stopped taking bowel-controlling drugs and have four or fewer bowel movements daily. Chemical hypokalemia requires, as a rule, liquid potassium supplementation for six months to one year; it is advisable to give all patients supplementary potassium upon discharge from the hospital. Chemical hypocalcemia requires oral calcium for six months to one year; extension of oral calcium intake indefinitely is recommended for the prophylaxis of oxalate kidney stones. Most patients need vitamin supplements; oral water soluble vitamins, vitamin A, and vitamin D for several years, and intramuscular vitamin B_{12}, 1,000 micrograms every six weeks, is continued for a lifetime. In addition, certain individuals may require magnesium supplements as well.

It is infrequent that side effects require take-down of the jejunoileal bypass. However, approximately 1 per cent of jejunoileal bypass patients may benefit from take-down for unremitting diarrhea or a persistent electrolyte abnormality.

Unique complications of jejunoileal bypass occur in 8 per cent of this population; 5 to 8 per cent of the total number of postoperative patients will require hospitalization for management and 2 to 3 per cent will require take-down or revision.[4, 6]

One of the most troublesome complications of jejunoileal bypass is gas-bloat syndrome and excessive flatulence. A wide spectrum of remedies has been employed, including bismuth subgallate, a lactose free diet, and antibiotics (tetracycline or metronidazole), singly, or in combination. An arthralgia-arthritis syndrome of an undefined origin occurs postoperatively, which is clinically and serologically distinguishable from rheumatoid and degenerative arthritis and usually responds to antibiotics and analgesics. Oxalate nephrolithiasis occurs when fatty acids and bile acids combine with intestinal calcium, resulting in an excess of absorbable oxalate, hyperoxalemia, and hyperoxaluria exceeding the formation coefficient for calcium oxalate stones. It has now been clearly demonstrated that patients maintained on 3.5 gm of oral calcium daily will be protected from this complication.[7] Nephrolithiasis can be a serious sequela of jejunoileal bypass surgery, occurring in approximately 10 per cent of postoperative patients; with indefinite calcium supplementation, this figure can be reduced to 2 per cent or less, the percentage prevalent in the population at large.[7]

Liver failure occurs in 5 per cent of jejunoileal bypass patients. These individuals will require hospitalization, often repetitively, for intravenous hyperalimentation, readjustment to adequacy of the oral protein intake and, possibly, establishment of a feeding jejunostomy for elemental protein administration into the proximal end of the bypassed segment for six months to one year. Despite these measures, 20 per cent of the patients with liver failure, or 1 per cent of the total number of postjejunoileal bypass patients, will require take-down of the bypass as a life-saving procedure. Experience has shown that patients who follow the prescribed diet of high protein and no alcohol will generally not experience liver failure.

When medical management of these jejunoileal bypass-engendered complications fails, take-down is recommended. Remedial surgery, how-

ever, should not be done in haste, and reoperation is preferably undertaken as a strictly elective procedure. Quite often this requires adequate preparation of the patient in hospital with hyperalimentation, supplemental oral protein, restoration of body electrolyte balance, and replenishing of body vitamin stores.

Generally, individuals undergoing take-down or revision of jejunoileal bypass have had an excellent weight response from the operation. This should be stressed; it is exceedingly rare that a patient will request a remedial operation for failure of weight loss after jejunoileal bypass.

Remedial Surgery

Early in the common experience with jejunoileal bypass, patients with life-threatening complications or with significant disturbance in the quality of life underwent bypass take-down only. Inevitably, after recovery all of these patients regained their original weight. Currently, unless the patient is extremely ill, jejunoileal bypass take-down without a concurrent gastric bypass operation to maintain the patient's weight response is not to be recommended.[8, 9, 16]

Also, operations that add length of bowel to the functioning segment are rarely performed today. Such operations may ameliorate certain syndromes, such as electrolyte imbalance, but they also generally result in a marked weight gain. Conversely, reducing the functioning small intestine in those rare patients justifiably requesting an additional weight response, meets with success in 50 per cent or less. Here too, it is probably advisable to take down the jejunoileal bypass and perform a concurrent gastric bypass procedure.

Technically, take-down of the jejunoileal bypass is not difficult, especially since in most cases the patient is then relatively thin. Entrance is gained into the peritoneal cavity through a high midline incision. All adhesions are carefully lysed. If the previous bypass has been an end-to-side jejunoileostomy, the jejunum is taken off the ileum, the antimesenteric ileal defect is closed transversely to prevent narrowing, and bowel continuity is restored by end-to-end jejunojejunostomy of the proximal bowel to the freshened proximal end of the previously bypassed segment.

If the jejunoileal bypass has been constructed end-to-end with a short ileal (4 cm) segment[3] the following steps are followed (Fig. 1): (1) the end-to-end anastomosis is taken down; (2) the distal ileum is closed at the ileocecal valve, preferably in two layers; (3) the proximal end of the bypassed segment is fashioned in such a manner as to provide the maximum surface for anastomosis of the atrophic bowel; and (4) end-to-end jejunojejunostomy reestablishes bowel continuity, with intestinal flow into the cecum via the original anastomosis for drainage of the end-to-side ileocecostomy for the then bypassed segment.

If the jejunoileal bypass consisted of end-to-end anastomosis of equal, or essentially equal, lengths of jejunum and ileum, with the bypassed segment drained into the sigmoid colon,[14] then an alternative approach is employed, as follows: (1) the end-to-end anastomosis is taken down; (2) the anastomosis into the sigmoid is taken down and the sigmoid is closed,

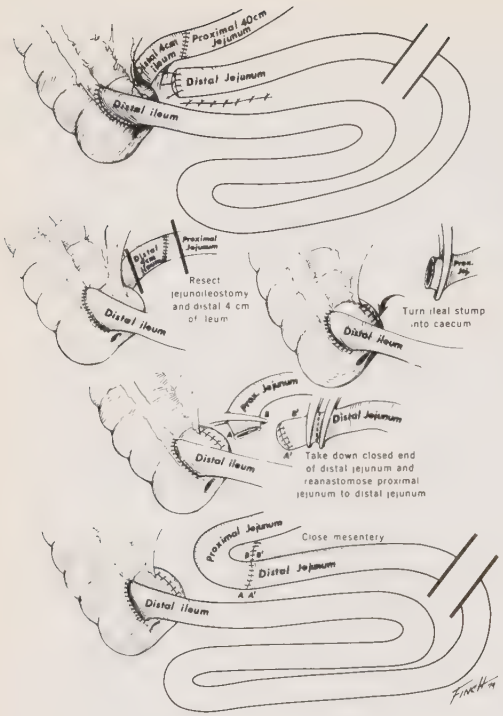


Figure 1. Take-down of an end-to-end jejunoileal bypass with a short ileal (4 cm) segment (see the text for details).

preferably in two layers; (3) the proximal end of the bypassed segment is, again, prepared in a manner to provide maximum surface for anastomosis; (4) end-to-end jejunojejunostomy reestablishes bowel continuity; and (5) physiological drainage of small intestinal contents is reestablished by end-to-end anastomosis of the distal end of the previously bypassed segment to the distal ileal segment.

Once take-down of the jejunoileal bypass is completed, a concurrent gastric bypass is performed, except in unusual situations, such as when the patient is in severe metabolic decompensation or advanced liver failure.

There are many ways to do a gastric bypass, or a gastroplasty, procedure. We prefer the following method, which is an adaptation of the method of Alden:[1] (1) the upper one-third of the greater curvature of the stomach is freed of all short gastric attachments in a retrograde manner and the spleen is carefully packed off posteriorly; (2) the lesser omentum is incised and the esophagus is encircled with a Penrose drain; (3) a second Penrose drain is passed around the stomach just distal to the first set of vessels on the lesser curvature; (4) using a comfortable length of jejunum, gastrojejunostomy is accomplished along the greater curvature of the stomach and its anterior wall just distal to the esophagogastric junction, using the GIA stapler device set at 0.7 cm; (5) after the previously inserted nasogastric tube has been passed well into the afferent

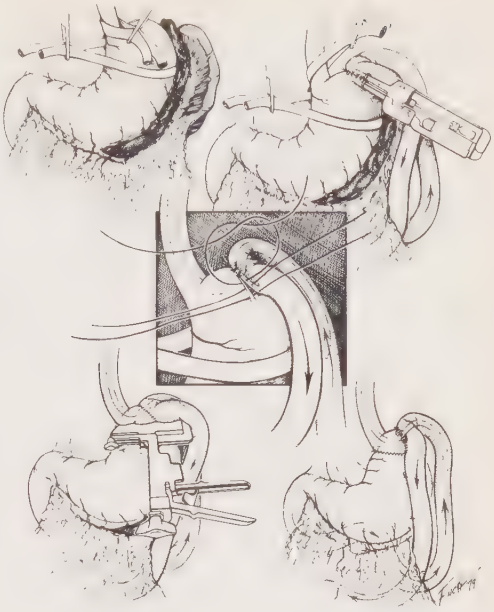


Figure 2. Construction of a gastric bypass with a 0.7 cm gastrojejunostomy and a 45-55 ml pouch (see the text for details).

loop, the gastrojejunostomy is closed with 5-0 permanent interrupted sutures, and the entire anterior and posterior surfaces of the anastomosis are oversewn with interrupted 5-0 permanent sutures; (6) the stomach is cross-stapled from the previously defined point on the lesser curvature in a line immediately below the anastomosis, leaving a less than 10 per cent (45 to 55 ml) pouch; (7) the corners of the gastric cross-stapling are reinforced with Z sutures; and (8) to complete the operation, the afferent and efferent loops of the jejunum are tacked to the stomach, above and below the anastomosis, to provide for a smooth contour and descent of bowel (Fig. 2).

After thoroughly irrigating the abdomen with an antibiotic solution and saline, closure is carried out with permanent interrupted sutures for the fascial layers, absorbable polyglycolic acid sutures for the subcutaneous fat, and fine skin approximation with a monofilament nylon. As a rule, it is best to leave at least one firm suction drain in the subcutaneous tissues, exiting through a separate stab wound and left in place for a minimum of five days on suction.

It is probably preferable to use previously functioning jejunum for the gastrojejunostomy, and not the previously bypassed segment, which is atrophic. For that reason, a Roux-en-Y anastomosis to the distal bowel is also avoided.

The final bowel arrangement for the jejunoileal bypass take-down with a concurrent gastric bypass, is illustrated in Figure 3.

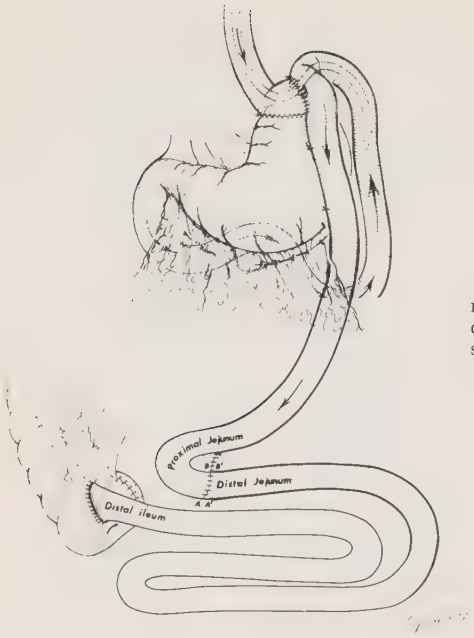


Figure 3. The final bowel arrangement following jejunoileal bypass takedown with concurrent gastric bypass is shown.

GASTRIC BYPASS

Causes of Failure

Today a family of gastric bypass or gastroplasty procedures exists, all based on the same therapeutic principle: restriction of the gastric capacity to precipitate satiety on minimal filling and physically to limit intake. The originator of gastric bypass is Dr. Edward Mason. He has experimented with this operation since 1966, switching every two to four years between various anastomotic bypasses and closure of the stomach, dividing the stomach into a small upper pouch and a large inferior pouch, and narrowing the egress from the upper pouch to the lower pouch to a small orifice (gastroplasty). Unfortunately, from the writings of Mason and Printen, one can only conclude that they maintain a perpetual, though admirable, dissatisfaction with their techniques.[10–13]

Currently, the two leading advocates of incomplete staple division of the stomach are Gomez, who calls his greater curvature conduit "gastroplasty," and Carey, who calls his central gastric orifice "gastric partitioning." These two procedures received a great deal of publicity, as well as advocates, prior to any official publication in the medical literature. Modifications of the anastomotic bypass and nonanastomotic incomplete gastric division have proliferated, and will continue to multiply.

Side effects of jejunoileal bypass are postprandial vomiting and distention early in the postoperative period, if intake is in excess of pouch size. There is, of course, a severely limited quantitative postoperative oral intake imposed by this procedure and, in some patients, qualitative di-

etary (low carbohydrate) restrictions must be maintained to prevent dumping. The specific need for vitamins or vitamin B_{12} injections or both has as yet not been established. It would be rare for a patient to require gastric bypass take-down for one of these side effects.

On the other hand, complications unique to gastric bypass occur in 5 to 8 per cent of patients, frequently requiring hospitalization, and necessitating bypass take-down or revision in 5 per cent of all gastric bypass patients. Complications include significant and unrelenting nausea and vomiting, afferent loop syndrome, chronic dumping syndrome, and, primarily, failure to lose weight.

The gastric bypass operation can be outeaten by any patient who undergoes this procedure. If the individual snacks on a continuous basis instead of confining himself to three or four set meals, only minimal weight loss will result from any of the gastric bypass procedures; indeed, no weight loss may occur, or weight may actually be gained.

It is too early to ascertain the failure rate that results from intrinsic technical inadequacies of these operations, such as disruption of the staple line, widening of the exiting orifice, distention of the adaptive pouch, and so forth.

Remedial Surgery

Most gastric bypass surgeons, those dedicated solely to the gastric bypass approach, have responded to a failed bypass by one or more attemps at revision. Thus, they reoperate, possibly two or three times, in order to narrow the out-flow tract from the stomach or reduce the size of the functional gastric pouch. We, on the other hand, unless the cause of the gastric bypass failure is reestablishment of continuity between the upper and the lower gastric pouch by pulling out of the staples or marked widening of a gastroplasty orifice, have found it more advisable to convert the patient to a jejunoileal bypass. Even in the above two circumstances, conversion to an untried mode of therapy for that individual patient seems worthy of consideration. It should be noted that individuals with failed gastric bypass signified by minimal weight loss more often than not have a barium x-ray determination of gastric pouch size and emptying time identical to those patients with a successful gastric bypass. We can only conclude from this, once again, that the primary cause of an insufficient weight response is not mechanical or technical in origin but results from the patient's eating habits.

Entrance is gained into the peritoneal cavity through the scar of the previous incision, usually a high midline approach. As a rule, it is best to ignore the failed gastric bypass or gastroplasty in the revision procedure. Regardless of the type of jejunoileal bypass preferred, the acceptable functional length of small bowel beyond the ligament of Trietz is 40 to 45 cm. When a gastrojejunostomy or a gastric bypass is present, therefore, the functional bowel must be measured along the efferent loop, or the Roux-en-Y limb, and should total about 65 cm to allow for the absence of duodenum in this new construction. Our standard jejunoileal bypass consists primarily of jejunum, with only a 4 cm sewing cuff of ileum. Although this operation originated with us in 1970,[3] recent evidence sup-

ports this choice of relative jejunal predominance as not only offering retention in continuity of the most proliferative absorptive surface but the one least likely to result in a lithogenic bile.[2, 15]

The appropriate bowel length (65 cm in this circumstance) is laid off along the mesenteric border, which is more consistent in length than the antimesenteric border. At the point of planned anastomosis, the bowel is divided. The distal end, the segment that will become the proximal end of the bypassed bowel, is closed in two layers; the two corner sutures and the middle suture of the outer interrupted row are not cut but left long. The ileum is divided 4 cm from the ileocecal valve. Anastomosis is performed between the proximal segment of jejunum and the distal ileum, end-to-end, as a two-layer open procedure. Next, the drainage anastomosis from the distal end of the bypassed segment is performed, end-to-side, into the cecum; again, as a two-layer open procedure. Finally, the two divisional and the one rotational mesenteric defects are carefully closed, and the previously retained sutures on the proximal end of the bypassed segment are used to tack that segment to the adjacent mesentery in order to prevent future intussusception (Fig. 4).

Under certain circumstances, it may be preferable to first take down the gastric bypass and then perform the jejunoileal bypass. Revision of the gastric bypass starts with take-down of the gastrojejunostomy. The gastric opening is not closed; on the contrary, it is extended along the anterior wall of the stomach of the upper gastric pouch. An incision of equal length is made in a parallel fashion in the inferior gastric pouch. Gastric continuity is then reestablished by gastrogastrostomy, in two layers, placing the cross-stapled line of the previous gastric partitioning posterior to the

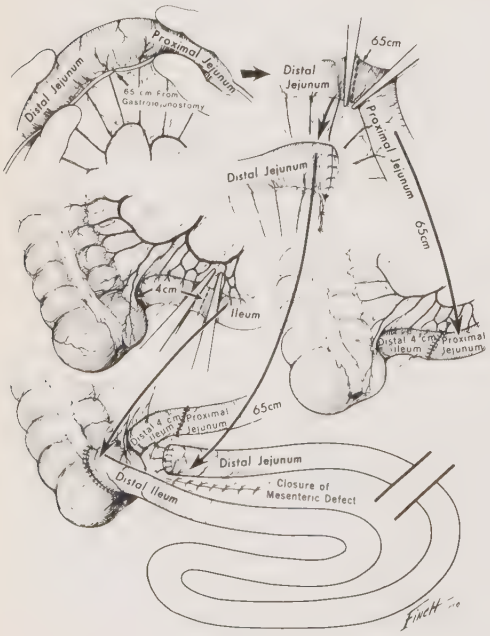


Figure 4. Construction of an end-to-end jejunoileal bypass starting with a gastric bypass in place and drainage of the bypassed segment into the cecum (see text for details).

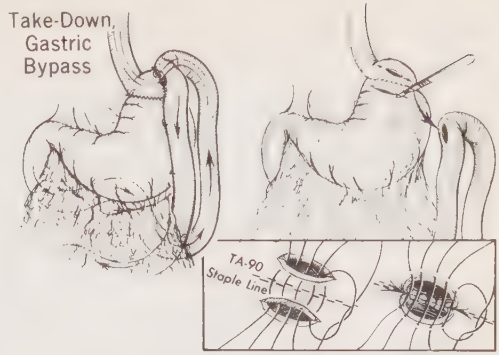
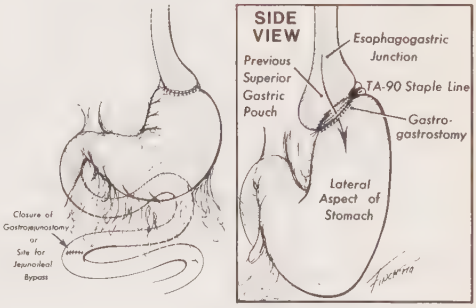


Figure 5. Take-down of a gastric bypass in preparation for a concurrent jejunoileal bypass (see text for details).



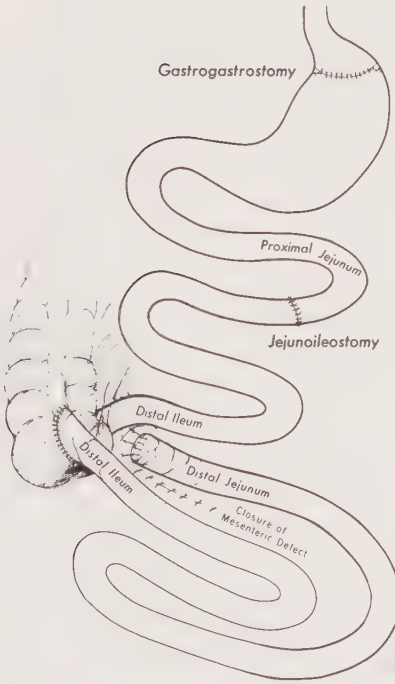


Figure 6. The final bowel arrangement subsequent to gastric bypass take-down with concurrent jejunoileal bypass.

back wall of the anastomosis (Fig. 5). When this procedure is performed, we prefer to employ the Scott operation for the jejunoileal bypass, utilizing the afferent loop for the proximal functioning intestinal segment.[14] Contrary to the original Scott operation, however, we construct the drainage anastomosis of the bypassed loop end-to-side into the cecum and not the sigmoid. The take-down of the gastric bypass, with concomitant jejunoileal bypass, is pictured in Figure 6.

Abdominal wall closure is comparable to that employed after jejunoileal bypass take-down and construction of a gastric bypass.

CONCLUSIONS

It is best, obviously, to perform the most suitable operation with the highest chance of success for each patient. Thus, the primary procedure for certain individuals should be a jejunoileal bypass and for others a gastric bypass. Adequate follow-up and patient cooperation, will, as a rule, prevent operative failure and the need for take-down and revision. Indeed, if the patient is thoroughly informed preoperatively of all untoward contingencies and methods for adequate postoperative self-care, if the patient is allowed to participate in selection of the operation, and if supportive and knowledgeable follow-up management is provided, reintervention is not likely to be necessary in more than 5 per cent of patients.

Fortunately, failure of the bypass, when it does occur, need not result in the necessity to maintain palliation, or in the acceptance of an inadequate weight response, or in a take-down alone and the inevitable regaining of the preoperative weight. The surgeon capable and willing to perform both jejunoileal bypass and gastric bypass can offer his patients suitable alternatives and a greater opportunity for ultimately achieving an adequate weight loss, free of serious complications, even if this outcome requires a conversion procedure from one bypass to the other.

REFERENCES

1. Alden, J. F.: Gastric and jejunoileal bypass: A comparison in the treatment of morbid obesity. Arch. Surg., *112*:799, 1977.
2. Bruusgaard, A., Sorensen, T., Justesen, T., et al.: Bile acid metabolism after jejunoileal bypass operation for obesity. Scand. J. Gastroenterol., *11*:833, 1976.
3. Buchwald, H., and Varco, R. L.: A bypass operation for obese hyperlipidemics. Surgery, *70*:62, 1971.
4. Buchwald, H., and Varco, R. L.: Metabolic intestinal bypass operations—Partial ileal bypass for hyperlipidemia and jejunoileal bypass for obesity. *In* Hardy, J. D. (ed.) Rhoads, Textbook of Surgery: Principles and Practices. Edition 5. Philadelphia, J. B. Lippincott Co., 1977.
5. Buchwald, H., Varco, R. L., Moore, R. B., et al.: Intestinal bypass procedures: Partial ileal bypass for hyperlipidemia and jejunoileal bypass for obesity. *In* Hardy, J. D. (ed.): Rhoads' Textbook of Surgery: Principles and Practices. Edition 5. Philadelphia, J. B. Lippincott Co., 1977.
6. Campbell, J. M., Hunt, T. K., Karam, J. H., et al.: Jejunoileal bypass as a treatment of morbid obesity. Arch. Intern. Med., *137*:602, 1977.
7. Clayman, R. B., Buchwald, H., Varco, R. L., et al.: Urolithiasis in jejunoileal bypass patients: The role of calcium carbonate. J. Urol., submitted for publication.
8. Hitchcock, C. T., Jewell, W. R., Hardin, C. A., et al.: Management of the morbidly obese patient after small bowel bypass failure. Surgery, *82*:356, 1977.
9. LaFave, J. W., and Alden, J. F.: Gastric bypass in the operative revision of the failed jejunoileal bypass. Arch. Surg., *114*:438, 1979.
10. Mason, E. E., and Ito, C.: Gastric bypass. Ann. Surg., *170*:329, 1969.
11. Mason, E. E., and Printen, K. J.: Gastric bypass for obesity. *In* Buchwald, H., and Varco, R. L. (eds.): Metabolic Surgery. New York, Grune and Stratton, 1978, ch. 2.
12. Mason, E. E., Printen, K. J. , Hartford, C. E., et al: Optimizing results of gastric bypass. Ann. Surg., *182*:405, 1975.
13. Printen, K. J., and Mason, E. E.: Gastric surgery for relief of morbid obesity. Arch. Surg., *106*:428, 1973.
14. Scott, H. W., Jr., Law, D. H., IV, Sandstead, H. H., et al.: Jejuno-ileal shunt in surgical treatment of morbid obesity. Ann. Surg., *171*:770, 1970.
15. Sorensen, T. I. A., Bruusgaard, A., Pedersen, L. R., et al.: Lithogenic index of bile after jejunoileal bypass operation for obesity. Scand. J. Gastroenterol., *12*:449, 1977.
16. Tapper, D., Hunt, T. K., Allen, R. C., et al.: Conversion of jejunoileal bypass to gastric bypass to maintain weight loss. Surg. Gynecol. Obstet., *147*:353, 1978.

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Vagotomy as a Treatment for Morbid Obesity

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VAGAL MEDIATION OF HUNGER

The importance of the vagus nerve for feeding behavior has been known since the late nineteenth century when Luciani demonstrated that transection of the vagal nerve abolished refeeding behavior in fasting dogs.[16] In spite of much experimentation in several species, including humans, the mechanisms for vagal regulation of feeding have not been fully elucidated. Both gastric (motility-related) and extra-gastric (effects of hormones on the central nervous system) stimuli of hunger seem to be mediated by the vagus, confounding the interpretation of weight decreases after vagotomy.

Truncal vagotomy of humans was introduced by Dragstedt et al. in 1944 as a treatment for ulcers.[6] Subsequently, after addition of a drainage procedure, it became a standard method in the treatment of duodenal ulcers. In the original clinical paper from 1944, the authors described reduction or abolition of hunger in some patients.[6] Later, in an attempt to determine the importance of insulin for hunger by studying vagotomized patients, Grossman and Stein[9] concluded: "vagotomy abolishes the gastric hunger pang without any significant effect on . . . the extra-gastric components." Vagotomy has been associated with weight loss in some series of duodenal ulcer patients,[12, 27] though it is difficult to assess the effects of the operation on "hunger" simply by studying body weight.

The most widely employed surgical method for treating obesity so far is jejunoileostomy. The ensuing weight decrease has been shown in several studies to be the result of decreased caloric intake due to unknown mechanisms.[4, 5, 19, 24] Gastric emptying of fluids by the technique of George[8] was studied in seven severely obese patients before and at intervals after end-to-side jejunoileostomy.[12a] The gastric emptying time was significantly delayed in all patients after the operation; this delay gradually decreased with time, almost reverting to preoperative levels of gastric emptying during the period of weight stabilization, when food intake is known to normalize. Furthermore, reduced preference for sweets[4] and

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other behavioral effects of jejunoileostomy are also similar to the effects of vagotomy[21] and may, in fact, be due to reduced vagal sensitivity, as suggested by Fox et al. based on experiments in rats.[7]

TRUNCAL VAGOTOMY IN OBESE PATIENTS

Between May 1977 and January 1979, truncal vagotomy without drainage was performed in 13 severely obese patients (11 females, 2 males) who were extensively screened before referral for surgical treatment of obesity according to commonly accepted indications.[3] Ten of the 13 patients were at their maximum body weight at the time of the operation (range, 111 to 142 kg). The other three patients had reduced by monitored dieting and physical exercise but had reached a plateau or had gradually started to regain, as always had been the case previously in all 13 patients. The patients all had combined hyperplastic-hypertrophic obesity, i.e., an excess of enlarged fat cells in comparison with controls. This type of obesity, with juvenile onset, has been shown to be associated with a mean yearly weight increase of 3 kg, irrespective of type of nonsurgical therapy.[11, 15] The patient data is summarized in Table 1. None of the patients had any history of ulcers, serious skull trauma, or gastrointestinal disorders; none regularly used any type of medicine. No one was overtly diabetic.

Methods

OPERATION. Truncal vagotomy was performed via an upper midline incision. The anterior and posterior vagal trunks were identified after mobilization of the esophagus. The trunks were followed as high as possible between the crura of the diaphragm and were cut under traction, about 3 cm of each trunk being resected for histologic verification. As an extra precaution, the hepatic nerve branches were cut and separate dissection of the esophagus was performed by the technique used for proximal selective vagotomy. No drainage procedure was performed. One patient (no. 3 in Table 1) originally underwent selective vagotomy of Latarjet's nerve, i.e., motor denervation, also without drainage; a year later she underwent completion of the truncal vagotomy.

ORAL GLUCOSE TOLERANCE TESTS with determination of plasma insulin levels were performed before the operation and at six-month intervals after the operation by previously described methods.[14]

GASTRIC ACID OUTPUT, measured as basal acid output after an overnight fast and peak acid output after injection of betazole (Histalog), was studied by routine methods before and at six-month intervals after the operation.

Results

BODY WEIGHT. A mean body weight decrease of 18.2 kg (range 2 to 64 kg) has been observed so far. In the eight patients studied for more than one year, the mean decrease has been 24 kg. Two patients seem to be failures: one (no. 6) has reduced only 2 kg from 129 kg during 13 months of observation; the other (no. 12) reduced 5 kg from 135 kg during six months

Table 1. *Postoperative Weight Loss of 13 Morbidly Obese Patients Treated with Truncal Vagotomy*

PATIENT NO.	AGE (YEARS)	PREOPERATIVE BODY WEIGHT (KG)	MAXIMUM BODY WEIGHT (KG)	POSTOPERATIVE WEIGHT LOSS (KG)	POSTOPERATIVE ASSESSMENT TIME (MOS.)	CLINICAL DATA
1	21	135		15	24	Pregnant, breast feeding
2	42	133	144	9	23	
3	41	103	108	34	23	Selective vagotomy and truncal vagotomy
4	29	137		23	22	
5	37	111		30	14	
6	29	129		2	13	Depression
7	29	142		64	12	
8	22	119		12	12	
9	23	112	114	10	8	Male
10	24	135		12	8	Male
11	47	90	116	2	8	Reduced before operation
12	40	135		5	6	Gastric hyposecretion
13	33	119		7	4	

of observation. Number 6 had an aggravation of earlier depressive symptoms soon after the operation and claims that she eats despite a lack of hunger sensation for want of "anything else to do." Number 12 reports hunger sensations just as before the operation. This patient had gastric hyposecretion preoperatively.

Three patients were not at their maximum body weight at the time of the operation (nos. 2, 3, and 11). The weight reduction after the operation in these patients concurs with observations on obese patients operated on by other procedures after weight reduction; namely, they lost less weight than they would have if operated upon at maximum weight. Since the vagotomy seems to have helped the patients to sustain weight reduction and even to lose some additional weight, the present postoperative loss could be considered "artifactually" low. Thus, the weight reductions of patients 2, 11, and 3 relative to their maximum weights are 20, 28, and 39 kg, respectively, in contrast to their actual losses of 9, 2, and 34 kg. The calculated mean reduction is 18.2 kg. The mean overall weight reduction (relative to maximum weight) of the 13 patients can thus be estimated to be 22 kg. For the eight long-term patients the relative maximum value is 29 kg. Apart from the net weight reduction, the operation could be considered to have prevented the yearly weight increases known to occur in these hyperplastic patients.[15]

The patient who had a selective motor nerve vagotomy at 103 kg (5 kg below her maximum weight) reduced 20 kg during the first six postoperative months. She then gradually started to regain, reporting "hunger" sensations. Eleven months after the first operation at a weight of 100 kg, she underwent a truncal vagotomy. During the following 12 months she lost 31 kg, or a total of 39 kg from maximum weight.

Two of the three patients observed for more than 22 months increased 9 kg above the minimum levels attained postoperatively, but their weight has been stable for at least six months. This, however, implies that longer periods of observation are necessary to evaluate the final results of the operation.

HUNGER SENSATIONS. All but one of the patients report a lack of "hunger," though several report "feelings of weakness" in the late afternoon after not having eaten any midday meal. These reports agree with the observations of Grossman and Stein[9] that vagotomy abolishes the insulin-induced gastric component of hunger (contractions) but does not influence feelings of emptiness and weakness. Some patients report "longing" or "craving" for something, though this feeling is not the same as "hunger." Several patients claim changes in taste preferences, though others have not noted any difference other than reduced food intake.

SIDE EFFECTS. Symptoms of gastric stasis such as foul-smelling eructations, and signs of residual stomach contents in studies of acid output, gastroscopy, and barium meals, have been noted. These side effects decrease with time. Occasional episodes of diarrhea have been encountered in three patients but no one has had chronic disabling diarrhea of the type that has been described after vagotomy. Barium x-rays have not revealed gastric dilatation or ulcers. Two of the patients have had single episodes of vomiting, in the one case due to "testing the limits," in the other to

"incautious eating." A majority of the patients complain periodically of fatigue, though many feel more physically active due to the reduced weight load.

GASTRIC ACID OUTPUT. The mean preoperative levels of basal acid output and betazole-stimulated acid output were higher than the reference values of the laboratory for age- and sex-matched controls (Table 2). The increased betazole-stimulated acid output is difficult to interpret but could reflect an increased parietal cell mass in patients with hyperplastic obesity. Significant reductions of both basal acid output and betazole-stimulated acid output after vagotomy have been found, but long-term results are lacking so far. Hollander tests for completeness of the vagotomy are difficult to assess, since the risk of understimulation is great, thereby confounding the results.

ORAL GLUCOSE TOLERANCE TESTS. Before the operation, the patients had hyperinsulinemia and glucose intolerance in comparison with age- and sex-matched controls (Table 3). After the operation, there was a significant reduction of total insulin and glucose levels to within the normal range.

Table 2. *Basal and Betazole-Stimulated Acid Output in 10 Severely Obese Patients Before and After Truncal Vagotomy*

ACID OUTPUT (mmol $HCl \cdot h^{-1}$)	BEFORE	AFTER	REFERENCE VALUE
Basal	4.7	2.4	3–4
range	0–7.2	0–3.8	
Betazole-stimulated	30	12.2	15–20
range	2–42	0.5–24	

Table 3. *Basal and Total Glucose and Insulin Levels During Oral Glucose Tolerance Tests in 10 Severely Obese Patients Before and After Truncal Vagotomy*[13]

	BEFORE	AFTER*	p
Basal glucose (mmol)	4.6 ± 0.3	4.0 ± 0.2 (3.7)	<0.05
Total glucose	29.6 ± 2.5	23.4 ± 1.1 (22)	<0.01
Basal insulin ($mU.1^{-1}$)	25.0 ± 3.6	15.1 ± 0.6 (10)	<0.05
Total insulin	386 ± 39	237 ± 18 (200)	<0.05

*Average values for 13 age- and sex-matched controls are given in parentheses.

MECHANISMS FOR WEIGHT DECREASE

Gastric

MOTILITY. Impaired gastric emptying would be the most obvious explanation for weight loss and is a predominant finding in these patients. Drugs that inhibit gastric emptying cause weight reduction but also have important metabolic effects that may affect body weight. Two groups of normal rats treated with truncal vagotomy, those with and those without drainage, lost the same amount of weight.[17] When rats with hypothalamic lesions underwent selective vagotomy, they did not lose a significant amount of weight,[23] which also implies that disturbed emptying is not sufficient to cause weight loss. Our patient treated with selective vagotomy did lose weight at first but subsequently regained most of it, which implies that impaired emptying is not sufficient to cause a sustained weight decrease. In contrast, truncal vagotomy in the same patient did lead to sustained weight loss.

Increased gastric tone[1] and impaired gastric adaptive relaxation[10] can explain a reduced capacity for eating, demonstrated by the patient who tried to "test the limits," and can also explain the reduced meal sizes in these patients.

ACID OUTPUT. It is difficult to isolate the importance of reducing gastric acid output in reduction of hunger sensations. There is no information about any correlation between gastric acid output and "hunger," though it is noteworthy that these obese patients had increased acid output compared with controls. The one patient with subnormal acid output before the operation does not seem to have been helped by truncal vagotomy during the first six months of observation.

Extra-gastric

Insulin is known to stimulate hunger by various mechanisms, both gastric and extra-gastric.[9] Experimental work has demonstrated that insulin has important central effects on appetite regulation.[28] In these hyperinsulinemic patients, vagotomy blunted the release of insulin and decreased the blood glucose level after oral ingestion of glucose. Possibly, the reduction in hyperinsulinemia reduces hunger.

Vagotomy influences other gastrointestinal hormones in addition to insulin, such as gastrin[26] and cholecystokinin,[25] which may be increased by the operation. Several studies have shown that cholecystokinin causes satiety, which also could explain some of the reduced hunger.[25]

Hypothetically, neural satiety mechanisms might be stimulated by vagotomy. Increased firing of hypothalamic neurons is induced by portal infusion of glucose, causing anorexia in fasted, vagotomized animals.[22] It has also been suggested that the vagus mediates glucoprivic or facilitatory information to the lateral hypothalamus, the hunger center, which thus could be attenuated by vagotomy.[18]

PATIENT SELECTION

Though this series is too small and the observation period too short to warrant extensive conclusions and recommend the procedure for general

use, some information can be gleaned from the experience so far. Screening of morbidly obese patients should include a gastrointestinal work-up with determination of acid output. Patients with hyposecretion probably should not be considered for vagotomy. The full cooperation of the patient is necessary, especially in overcoming habitual eating (dissociated from "hunger") or eating as a behavioral disorder, used to "treat" emotional problems. The most successful patients so far insist that they are *consciously* weight-reducing but that it is much easier after the operation than it ever had been previously. Alcoholism is a contraindication, as in all forms of surgery for obesity. Potentially, patients with proven hypothalamic obesity should benefit from truncal vagotomy, though a drainage procedure or antrectomy might be required, depending on the acid output and the increased risk of ulcer formation in such patients.

SUMMARY

Based on animal experiments,[20] on the original clinical observations of Dragstedt,[6] and on similarities with appetitive behavior after jejunoileostomy,[3] truncal vagotomy has been attempted as a treatment for morbid obesity in 13 patients with a mean weight of 123 kg. Weight decreases of 20 to 30 kg (range, 2 to 64 kg) have been observed so far. Impaired gastric emptying alone does not seem to account for the decreases. Possibly, improved glucose tolerance with reduction of hyperinsulinemia and other hormonal and/or neural effects are responsible for weight loss and lack of "hunger."

The period of observation is short, yet 2 of the 13 patients seem to be failures, of whom one had gastric hyposecretion before operation. It is too early to consider the procedure for general clinical use, which must await further research efforts.

REFERENCES

1. Aune, S.: Intragastric pressure after vagotomy in man. Scand. J. Gastroenterol., *4*:447, 1969.
2. Barry, R. E., et al.: Intestinal adaptation after jejunoileal bypass in man. Am. J. Clin. Nutr., *30*:32, 1977.
3. Bray, G. A.: The Obese Patient. Philadelphia, W.B. Saunders, 1976.
4. Bray, G. A., et al.: Food intake and taste preferences for glucose and sucrose decrease after intestinal bypass surgery. *In* Novin, D., Wyrwicka, W., and Bray, G. (eds.) Hunger: Basic Mechanisms and Clinical Implications. New York, Raven Press, 1976.
5. Condon S. C., et al.: Role of caloric intake in the weight loss after jejunoileal bypass for obesity. Gastroenterology, *74*:34, 1978.
6. Dragstedt, L. R., et al.: Supra-diaphragmatic section of the vagus nerves in the treatment of duodenal and gastric ulcers. Gastroenterology, *3*:450, 1944.
7. Fox, K. A., et al.: Dietary self-selection following sub-diaphragmatic vagotomy in the white rat. Am. J. Physiol., *231*:1790, 1976.
8. George, J. D.: New clinical method for measuring the rate of gastric emptying: The double sampling test meal. Gut, *9*:237, 1968.
9. Grossman, M. I., and Stein, I. F.: Vagotomy and the hunger-producing action of insulin in man. J. Appl. Physiol., *1*:263, 1948.
10. Jahnberg T., et al.: Dynamic gastric response to expansion before and after vagotomy. Scand. J. Gastroenterol., *10*:593, 1975.
11. Johnson, D., and Drenick, E. J.: Therapeutic fasting in morbid obesity. Long term follow-up. Arch. Intern. Med., *137*:1381, 1977.
12. Johnson, H. D., et al.: The late nutritional and haematological effects of vagal section. Br. J. Surg., *56*:4, 1969.

12a. Kral, J. G., and Faxén, A.: Unpublished observations.

13. Kral, J. G., Lundholm, K., Björntorp, P., et al.: Hepatic lipid metabolism in severe human obesity. Metabolism, *26*:1025, 1977.
14. Kral, J. G., et al.: Body composition and adipose tissue cellularity before and after jejunoileostomy in severely obese subjects. Eur. J. Clin. Invest., 7:413, 1977.
15. Krotkiewski, M., et al.: Adipose tissue cellularity in relation to prognosis for weight reduction. Int. J. Obesity, *1*:395, 1977.
16. Luciani, L.: Das Hungern, Leipzig 1890. *In* Carlson, A. J. (ed.): The Control of Hunger in Health and Disease. Chicago, 1916.
17. Mordes, J. P., et al.: Decreased weight gain and food intake in vagotomized rats. Proc. Soc. Exp. Biol. Med., *156*:257, 1977.
18. Novin, D.: Visceral mechanisms in the control of food intake. *In* Novin, D., Wyrwicka, W., and Bray, G. (eds.): Hunger: Basic Mechanisms and Clinical Implications. Raven Press, New York, 1976.
19. Pilkington, T. R. E., et al.: Explanations for weight loss after ileojejunal bypass in gross obesity. Br. Med. J., *1*:1504, 1976.
20. Powley, T. L., and Opsahl, C. A.: Ventromedial hypothalamic obesity abolished by subdiaphragmatic vagotomy. Am. J. Physiol., *226*:25, 1974.
21. Rezek, M., et al.: Insulin dependence of paradoxial overeating: Effect of mannoheptulose, somatostatin, and cycloheximide. Am. J. Physiol. *236*:E205, 1979.
22. Russek, M.: Participation of hepatic glucoreceptors in the control of intake of food. Nature, *197*:79, 1963.
23. Sawchenko, P. E., et al.: Effects of selective subdiaphragmatic vagotomies on knife cut induced hypothalamic hyperphagia. Abstracts Sixth International Conference Physiology Food and Fluid Intake, Paris, 1977.
24. Sclafani, A., et al.: Effects of intestinal bypass surgery on appetite, food intake, and body weight in obese and lean rats. Am. J. Physiol., *234*:E389, 1978.
25. Smith, G. P., and Gibbs, J.: Cholecystokinin and satiety: Theoretic and therapeutic implications. *In* Novin, D., Wyrwicka, W., and Bray, G. (eds.): Hunger: Basic Mechanisms and Clinical Implications. New York, Raven Press, 1976.
26. Stadil F., and Rehfeld, J. F.: Gastrin response to insulin after selective, highly selective, and truncal vagotomy. Gastroenterology, *66*:7, 1974.
27. Wheldon, E. J., et al.: Late metabolic sequelae of vagotomy and gastroenterostomy. Lancet, *1*:437, 1970.
28. Woods, S. C., and Porte, D.: Insulin and the set-point regulation of body weight. *In* Novin, D., Wyrwicka, W., and Bray, G. (eds.): Hunger: Basic Mechanisms and Clinical Implications. New York, Raven Press, 1976.

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Plastic Reconstruction after Bypass Surgery and Massive Weight Loss

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Massive weight loss achieved by either dieting or surgical means can produce a much improved body image for the patient. However, the folds of excess skin that develop with weight loss can be very disturbing to the patient and, to a great extent, psychologically negate the many beneficial effects of the weight loss. As in all cosmetic surgery, there is no direct relation between the actual degree of abnormality or disfigurement and the magnitude of the patient's psychological response to it.

Furthermore, it must be appreciated that by their sheer weight, folds of excess skin and subcutaneous tissue can be directly responsible for pain (e.g., low back syndrome), unbalanced supportive tissue stress, and skin irritation and infection. Thus, after the massive weight loss that can follow bypass surgery, nonpsychological problems can ensue secondary to residual skin that require attention and, possibly, therapeutic intervention.

For the majority of patients who have experienced massive weight loss, the general improvement in well-being outweighs the persisting problems of deformities due to marked excesses of skin. A minority of patients will be encumbered by deformities of the breast, abdomen, or extremities and will seek further surgery. Operative procedures that can substantially ameliorate problems in each of these areas are now available. All of these techniques constitute major surgical operations involving general anesthesia, significant blood loss, and hospitalization for several days. The risks of this type of body-contouring surgery are thus greater than the risks associated with other types of cosmetic surgery, such as facial plasty or augmentation mammoplasty, which can be done under local anesthesia with short recovery time.

BREAST

Following massive weight loss, deformities of the breasts are largely due to ptosis and, to a lesser extent, mammary hypertrophy. If the patient

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had small- to medium-sized breasts prior to weight gain and loss, the aesthetic problem will be ptosis resulting from excess skin. If the patient had large breasts prior to the weight gain and loss, cosmetic correction will require reduction of the breast mass as well as reduction of the size of the skin envelope. There are certain physical indications for reconstructive breast surgery in addition to the psychological consideration of the desire for a more normal breast shape. The patient with excessively large breasts will be subject to upper back and neck pain due to postural problems caused by the large breasts. She may experience pain in the shoulder area due to excessive weight of the breasts on the brassiere straps, and there may be persistent intertrigo in the constantly moist skin folds in the inframammary area.

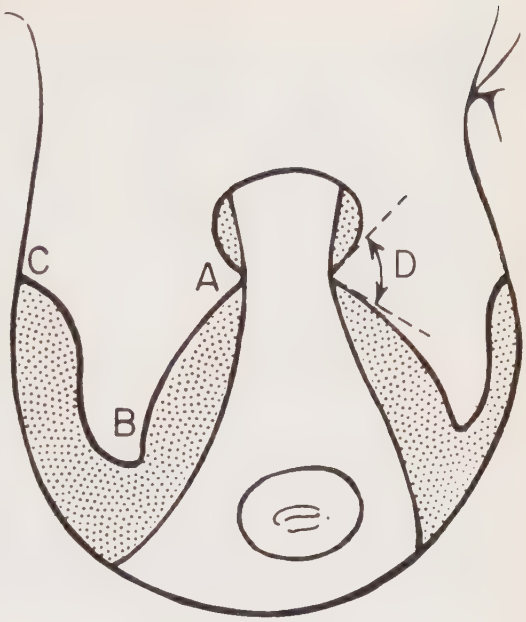
Although techniques of breast reduction and reconstruction date back to Hippocrates, who described amputation of the breast with hot cautery,[1] the multitude of techniques and procedures described prior to the last 25 years are of historical interest only. In 1956 Wise presented a pattern for planning reduction mammoplasty.[20] This use of a preoperative marking pattern, which was based upon the principle of the creation of a skin brassiere, provided for the first time a standardized guideline from which the remainder of the operation involving breast tissue resection could be derived. The method of breast resection advocated by Wise was, however, not widely used. In 1960 Strombeck published a technique employing the Wise pattern and a transverse dermal pedicle for vascular support of the nipple-areola complex.[17] The Strombeck technique gained immediate wide acceptance. Certain minor problems were evident with the Strombeck technique. Nipple inversion was frequent and transposition of the nipple was difficult in large reductions because of the limitations of the transverse pedicle.

In 1972, McKissock published a variation of the Strombeck technique that involved the use of a vertical dermal pedicle and a different configuration of breast resection.[11] The use of a vertical dermal pedicle made upward transposition of the nipple-areola complex easier in large reductions. Weiner has shown that the McKissock technique can be modified by the use of a single attachment of the vertical dermal pedicle superiorly to provide greater flexibility in the operative technique.[19] We believe the McKissock technique is the method of choice for both reduction mammoplasty and mastopexy.[12] This technique is illustrated in Figures 1 through 4.

Aesthetically attractive breasts can result from this reduction mammoplasty technique. The lower size limit to which the breasts can be reduced and still maintain a good breast contour is approximately the B-cup size.

Inevitable consequences of the operation involve a decrease in sensibility of the nipple-areola complex and changes in sensibility in the dissected areas of the breast. Complications of the procedure include hematoma, skin slough, and infection. The complication rate is proportional to the amount of breast tissue resected. In resections of less than 500 gm per breast, the complication rate is very low. In massive resections, the complication rate can approach 15 per cent.[18]

Figure 1. Prior to the induction of general anesthesia, the patient is placed in the sitting position. Inspection of the breasts will allow an estimation of the amount of breast tissue to be resected and the extent to which the procedure is one of reduction mammoplasty or ptosis correction. The midline of the breast and the inframammary fold are marked. A new position for the nipple is chosen at a point 19 to 22 cm from the suprasternal notch. This point should conform to the level of the midhumerus and the underlying inframammary fold. The midline of the breast is usually established on a line from a point on the clavicle 7 to 8 cm from the suprasternal notch to a point in the inframammary fold at a point 8 to 9 cm from the midline. The Wise keyhole pattern is then used to outline the new areola and the design of the skin resection. A series of Wise patterns with variation at angle D are used and selected on the basis of breast configuration. Critical points in the resection outline are measurement of the distance from the areola to the inframammary fold (A-B), which should be 5 to 6 cm, and creation of a lazy-S configuration in the lower margin of the upper medial and lateral skin flaps (B-C). A vertical dermal pedicle 6 cm wide is outlined.



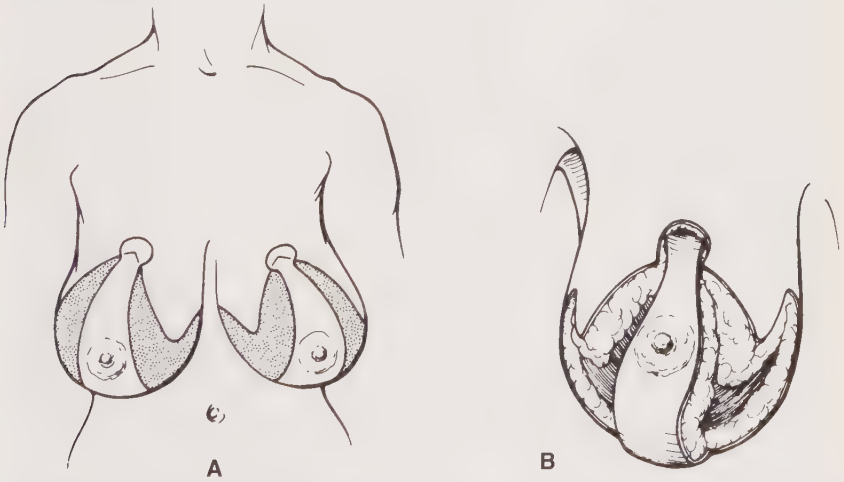


Figure 2. *A*, The shaded areas represent areas of skin and breast tissue resection. The areolar pedicle in deepithelialized. If the procedure is a mastopexy rather than reduction mammoplasty, only skin is resected in the medial and lateral quadrants. *B*, The dermal pedicle is thinned. Adequate resection of breast tissue deep to and superior to the new location of the nipple must be accomplished for proper contouring of the reconstructed breast.

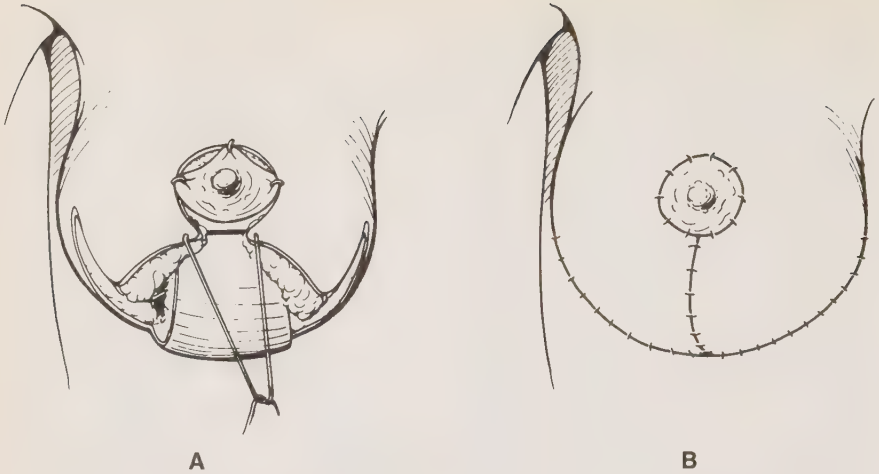


Figure 3. *A*, Tacking sutures of 4–0 nylon are placed about the areola and in the lower incisions. A Jackson-Pratt suction drain is placed in the wound. *B*, The wound is closed with a running 3–0 proline subcuticular suture in the incision in the inframammary fold and in the incision extending from the areola to the inframammary fold. Subcutaneous sutures are not used. Interrupted 6–0 nylon sutures are placed about the areola, and a running 6–0 nylon suture is used at the skin edge. The drain is removed at two days. The 6–0 nylon sutures are removed at four to seven days, and steri-strips are applied. The subcuticular sutures are removed at three weeks. The patient is maintained in a stretch brassiere for three weeks. Moderate restriction of activity is suggested for three weeks.

Figure 4. Preoperative (*A* and *B*) and postoperative (*C* and *D*) views of patient who underwent reduction mammoplasty using the techniques described.

ABDOMEN

The distorted abdominal wall may be one of three shapes—flaccid, rounded, or pendulous (with or without stria). Other problems to be considered are the presence of operative scars, ventral hernias, and diastasis recti.[12]

Techniques of abdominoplasty can be classified on the basis of the direction of the scar. Babcock described a vertical excision technique.[3] Kelly, who first described techniques of abdominoplasty in 1910, used a transverse method.[8] Mixed techniques using both horizontal and vertical incisions have been reported by Castanares and Goethel.[6] Only a technique that leaves a horizontal scar can produce a truly acceptable aesthetic result in the abdomen. The transverse technique described by Pitanguy represents the best technique for correction of deformities of the abdomen.[10, 14, 15] This technique is illustrated in Figures 5 through 13.

Pitanguy has analyzed the results of 539 consecutive abdominoplasties.[15] There were 77 complications, including 32 patients with serosanguinous collections, 20 patients with hypertrophic scars, and 10 patients with some degree of flap necrosis. There were no life-threatening complications. It should be noted that this series of patients constituted primarily a thin to moderately obese group. Complication rates can be expected to be higher in patients who have sustained massive weight loss.

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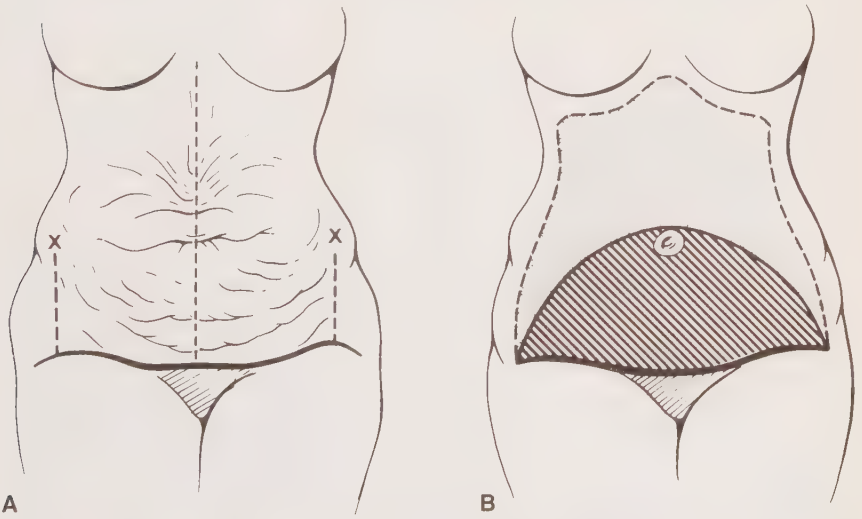

Figure 5. *A*, The midline of the abdomen is marked from the xiphoid process to the pubic bone. The anterior superior iliac spines are marked X, and perpendicular lines are drawn downward. A transverse incision is outlined at the superior margin of the pubic hair medially. Laterally, the incision curves down slightly and extends beyond the line of the anterior superior iliac spine for 4 to 6 cm. *B*. In patients in whom there is marked excess skin of the abdominal wall, all of the tissue between the transverse line of incision and the level of the umbilicus can be excised. The abdominal wall flap is undermined at the supra-aponeurotic plane. The flap is divided in the midline to the level of the umbilicus, and the skin of the umbilicus is carefully circumscribed, preserving a vascular pedicle. The abdominal wall flap is undermined superiorly to the costal margin. The undermining can be done rapidly using a cutting cautery. Large perforating vessels should be tied.

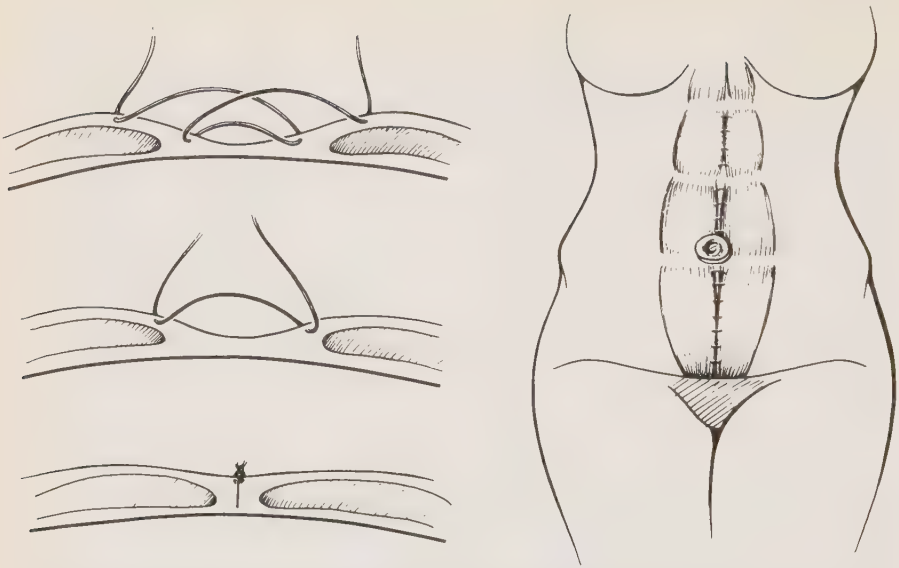

Figure 6. Correction of the separation of the rectus muscles and ventral hernia is accomplished following elevation of the skin. Most patients will require plication of the rectus fascia from the xiphoid process to the pubic bone. Either simple or figure-of-eight 2–0 nonabsorbable sutures are used.

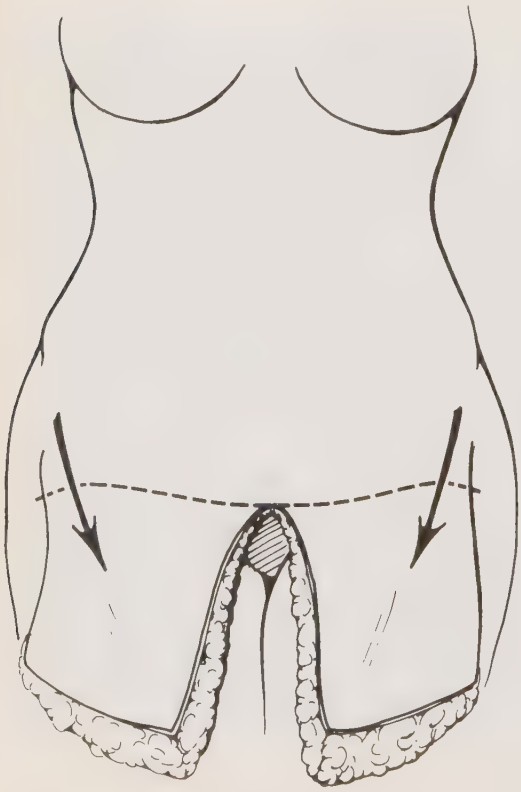

Figure 7. The operating table is flexed approximately 30 degrees at the hips, and the abdominal wall skin flap is pulled inferiorly and medially. A central tacking suture is placed, and the excess skin is trimmed from each half of the abdominal wall flap. Excessive subcutaneous tissue at the lower border of the flap can be trimmed.

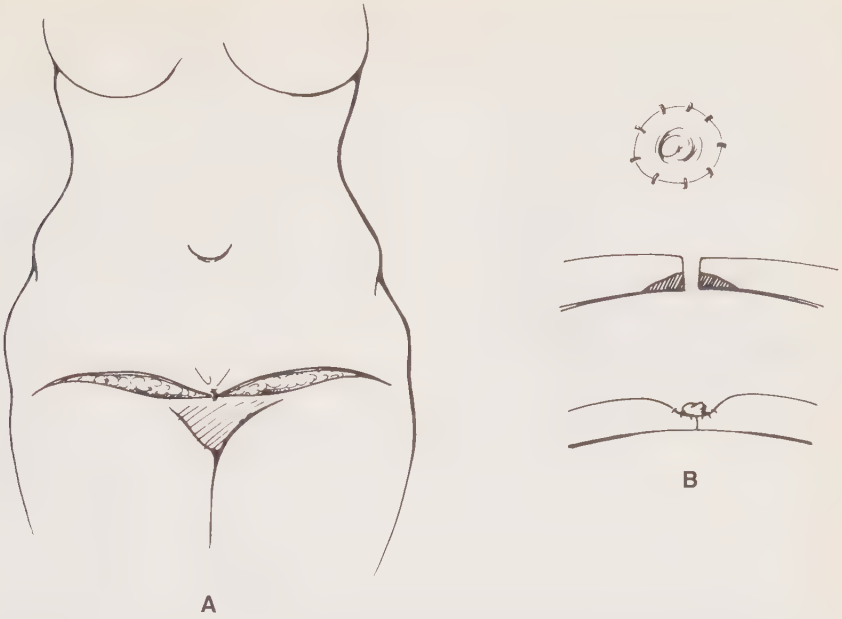

Figure 8. *A*, With the new configuration of the abdominal wall established, a 2-cm, curving transverse incision is made in the skin flap at the level of the umbilicus. *B*, Excessive subcutaneous tissue at this level can be trimmed to provide a normal depressed appearance of the umbilicus when sutured in place.

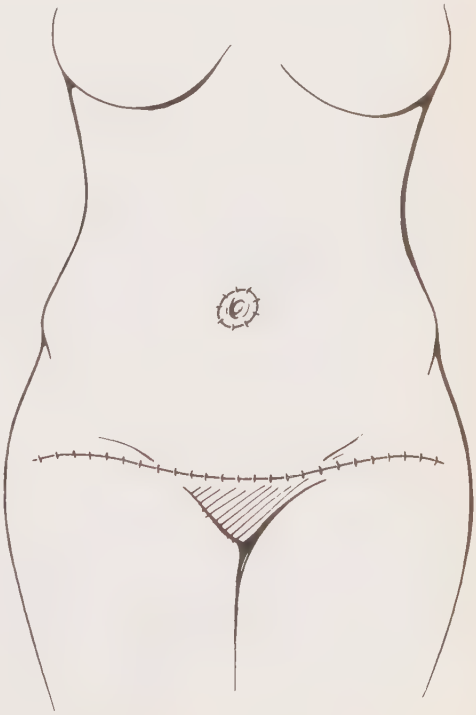

Figure 9. The wound is closed in layers with interrupted 2–0 dexon sutures in the subcutaneous tissues and a running 3–0 proline subcuticular suture at the dermal level. A running 6–0 nylon suture is used at the skin edge. Interrupted 6–0 nylon sutures are used around the umbilicus. Bilateral Jackson-Pratt suction drains are placed. The patient is maintained at bed rest with bathroom privileges for three to four days postoperatively. Compressive dressings are not used. Drains are removed on the second or third day. The 6–0 nylon sutures are removed at four to seven days. The subcuticular sutures are removed at three weeks.

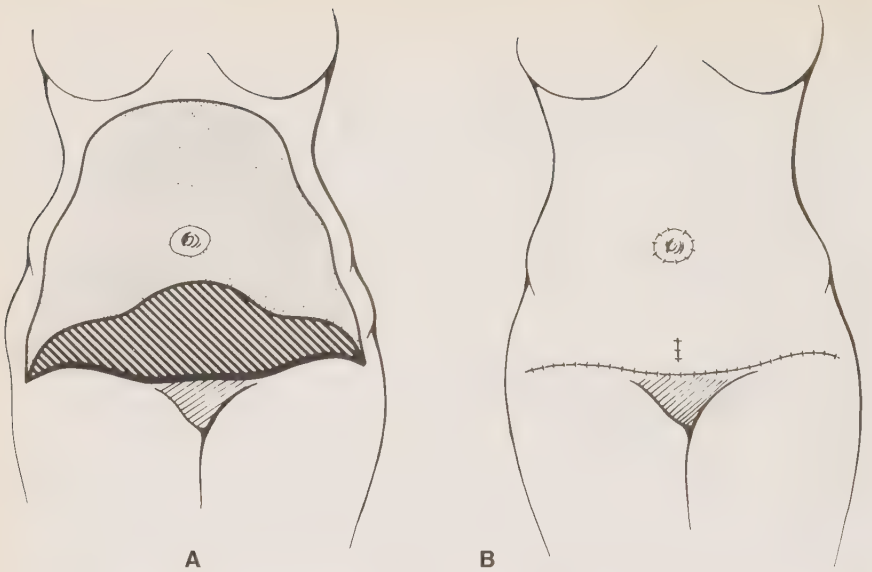

Figure 10. *A*, There are several variations in this basic technique, which can be used depending upon the abdominal wall deformity. It may not be possible to excise all of the tissue between the umbilicus and the transverse incision in patients in whom the skin excess is of moderate degree. *B*, The final result is a small vertical midline scar representing the closure of the original umbilicus position in the overlying abdominal skin flap.

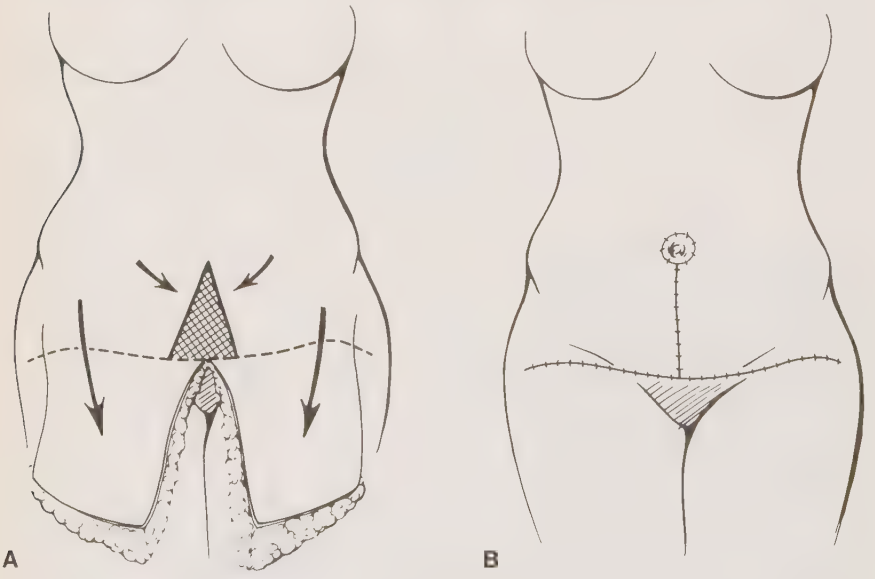

Figure 11. *A*, If the patient has massive skin excesses at the lateral margins of the abdomen, more effective contouring of the waistline area can be accomplished by employing a midline wedge excision of tissue in the area superior to the original location of the umbilicus. *B*, The result is a T-shaped closure. If at all possible, vertical components of the incision are to be avoided. Vertical scars are not as satisfactory in appearance as transverse scars in the lower abdominal area. In addition, skin vascularity in the medial corners of the abdominal flaps can be compromised, leading to delayed healing at the junction of the vertical and transverse incisions.

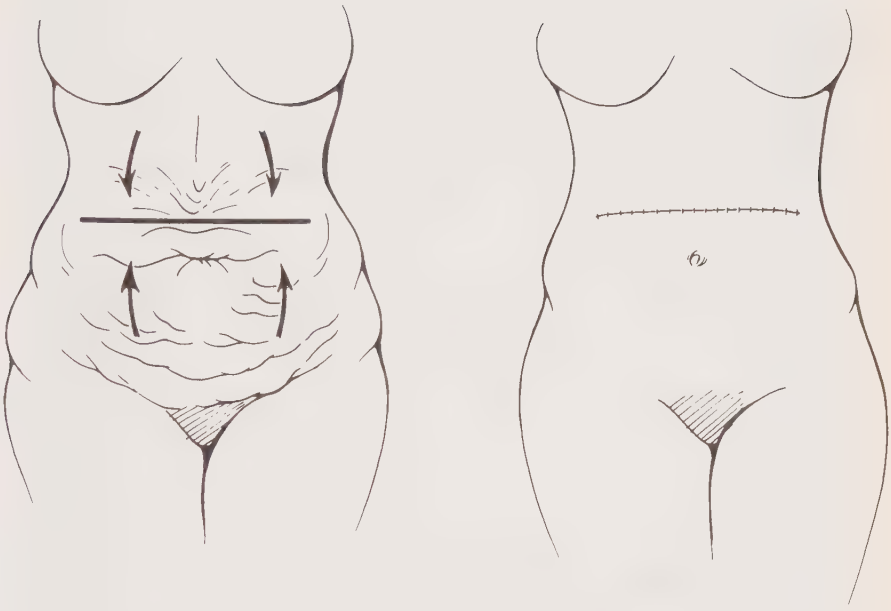

Figure 12. Techniques of upper abdominoplasty described by Baroudi et al.[4] and Rebello and Franco[18] employ a transverse upper abdominal incision. This type of resection very adequately tightens the epigastric area but is less effective for overhanging folds of skin of the lower abdomen. However, this technique should be considered in patients who have previously had a transverse upper abdominal incision. In most cases, we would prefer to use the lower transverse abdominal incision with transposition of the old incision to the lower abdomen, thus leaving the upper abdominal area without visible scars.

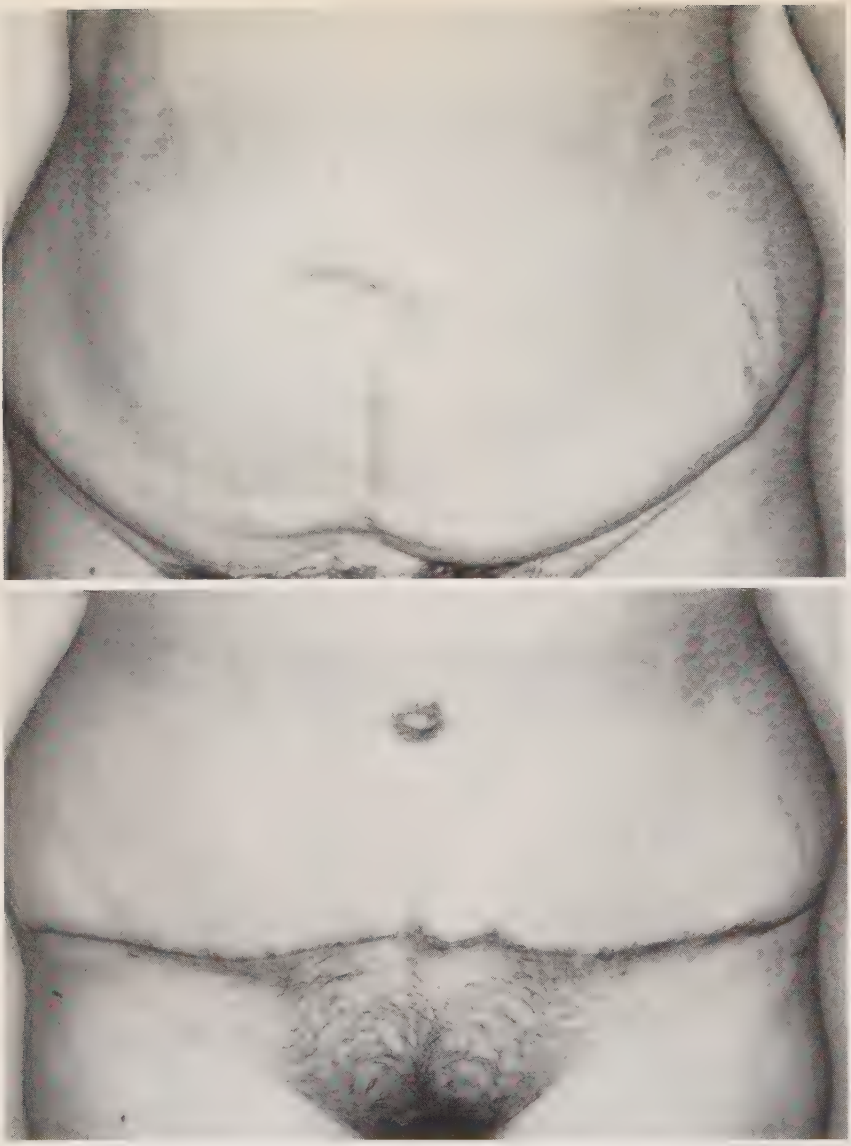

Figure 13. Preoperative (above) and postoperative (below) views of patient who underwent abdominoplasty by the technique described.

THIGHS AND BUTTOCKS

Excessive fat deposits are common in the trochanteric areas, and marked excesses of skin may develop in the posterior buttock and medial thigh areas. Surgical procedures for the reduction of excess skin of the thighs and buttocks are, in general, less satisfactory than procedures for the breast or the abdomen.[7, 9, 10, 13] The deformities are often only partially corrected, and the scars can be noticeable and occasionally painful. The technique is illustrated in Figures 14 through 17.

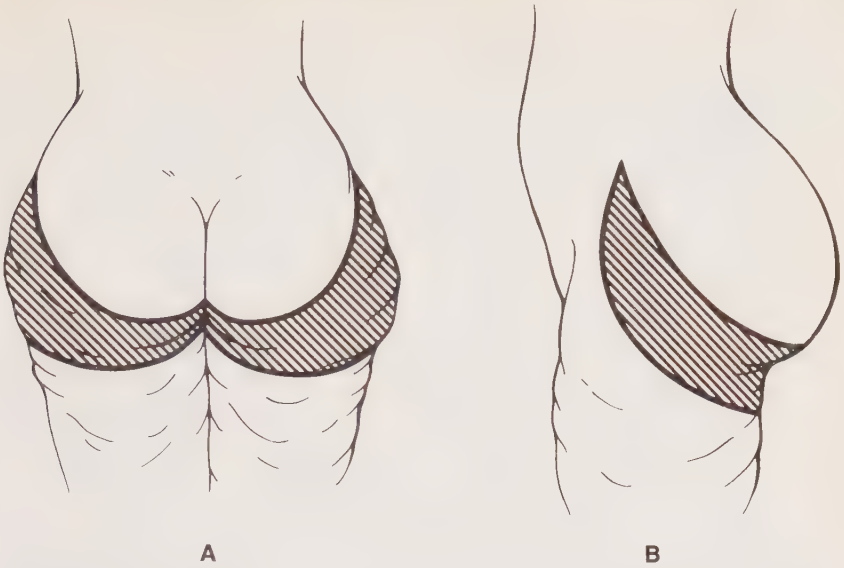

Figure 14. *A*, The patient is examined and marked in the standing position. If excessive skin of the buttock area is the sole problem, a transverse elliptical incision placed in the skin fold at the lower portion of the buttock is outlined. *B*, Laterally, the excision can be carried into the trochanteric area if there are significant deposits of subcutaneous tissue and excess skin.

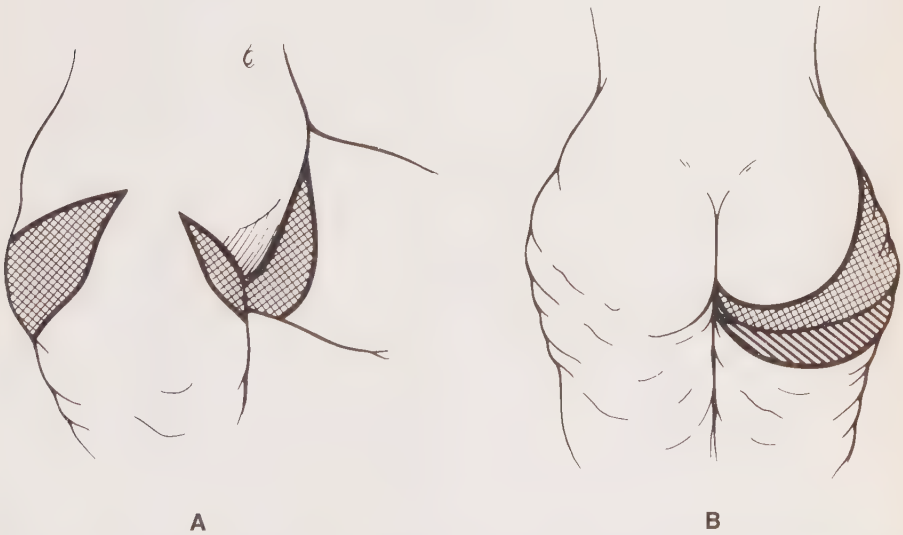

Figure 15. *A*. The buttock excision is combined with a medial thigh excision for moderate excesses in the proximal medial thigh. *B*. Agris has suggested use of a deepithelialized area (parallel marking) of the thigh flap that is buried beneath the buttock skin to aid in wound closure and support.[2]

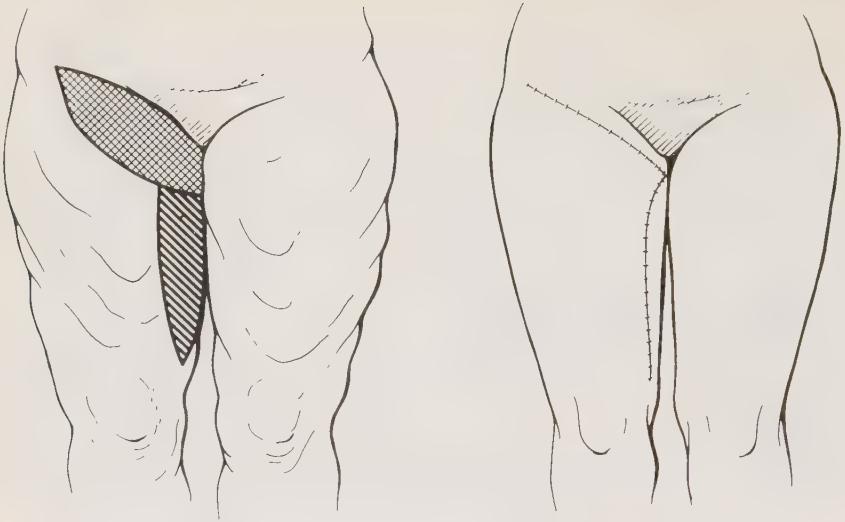

Figure 16. Marked skin excesses in the medial thigh are corrected by more extensive upper thigh resections. An extension of the resection can be carried out in the distal medial thigh (parallel marking). General anesthesia is used. The prone position is used if posterior buttock resection only will be done. A lithotomy position is preferred for the inner thigh area. Skin and subcutaneous tissue are resected. In the medial thigh area, the saphenous vein should be preserved, whereas the superficial external pudendal artery and vein and the superficial epigastric artery and vein are sacrificed.

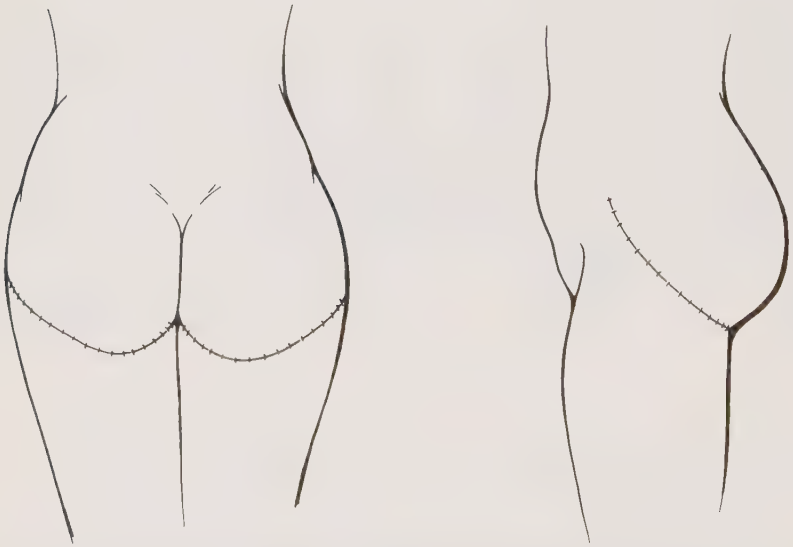

Figure 17. The wounds are closed in layers using interrupted 2–0 dexon sutures in the subcutaneous tissues and a running 3–0 proline subcuticular suture at the dermal level. A running 6–0 nylon suture is used at the skin edge. Jackson-Pratt suction drains are placed. The 6–0 nylon sutures are removed at four to seven days and the subcuticular sutures at three weeks.

ARMS

Skin redundancy in the arm can cause problems with the fit of clothes in the sleeve area. Excess skin of the arm can be excised; however, the resection necessitates a longitudinal incision that leaves a noticeable scar.[10, 15] The technique is illustrated in Figures 18 and 19.

Figure 18. With the patient in the upright position and the arms extended, excess skin of the arm is estimated and marked. An elliptical resection is outlined on the posterior aspect of the arm at the junction with the medial aspect to place the scar in the least conspicuous position. A Z-plasty may be performed in the area of the axilla anteriorly or posteriorly.

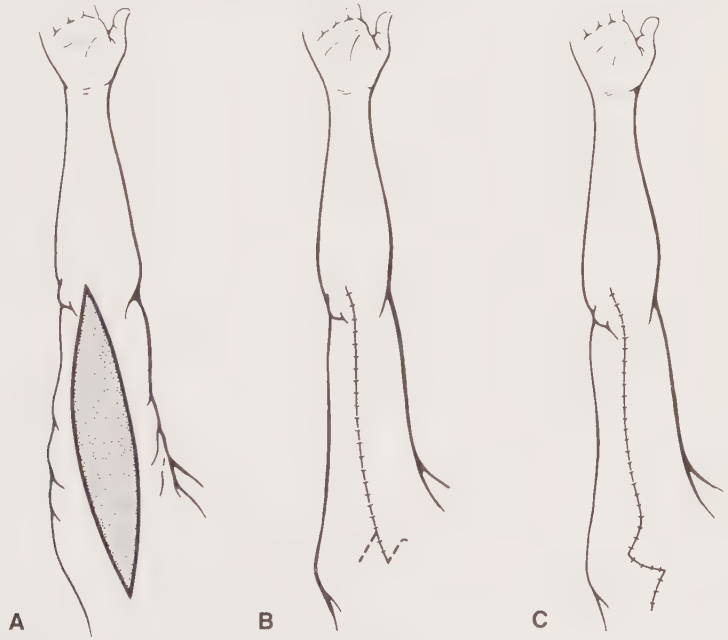

Figure 19. *A* and *B*, The wound is closed in layers using interrupted 3–0 dexon sutures in the subcutaneous tissue and a running 3–0 proline subcuticular at the dermal level. A running 6–0 nylon suture is used at the skin edge. *C*, Care must be used in the design of the axillary Z-plasty to avoid transposition of hair-bearing skin to a conspicuous location.

SUMMARY

In summary, the surgical techniques described can provide substantial benefit to selected patients who have sustained massive weight loss. As in all cosmetic surgery, patient selection must be meticulous. The expectations of the patient must be realistic, and the very real risks of the operative procedures must be understood. Patients who have sustained massive weight loss should be informed of the possibilities of reconstructive plastic surgery.

REFERENCES

1. Adams, F.: The Genuine Works of Hippocrates: On Air, Waters, and Places. Syndenham Society, London, 1849, vol. 1, p. 221.
2. Agris, J.: Use of dermal-fat suspension flaps for thigh and buttock lifts. Plast. Reconstr. Surg., *59*:817, 1977.
3. Babcock, W.: On diseases of women and children. Am. J. Obstet., *74*:596, 1916.
4. Baroudi, R., Keppke, E. M., and Carvalho, C. G.: Mammary reduction combined with reverse abdominoplasty. Ann. Plast. Surg., *2*:368, 1979.
5. Baroudi, R., Keppke, M., and Netto, F. T.: Abdominoplasty. Plast. Reconstr. Surg., *54*:161, 1974.
6. Castanares, S., and Goethel, J. A.: Abdominal lipectomy: A modification in technique. Plast. Reconstr. Surg., *40*:378, 1967.
7. Hoffman, S., and Simon, B. E.: Experience with the Pitanguy method of correction of trochanteric lipodystrophy. Plast. Reconstr. Surg., *55*:551, 1975.
8. Kelly, H. A.: Excision of the fat of the abdominal wall-lipectomy. Surg. Gynecol. Obstet., *10*:229, 1910.
9. Lewis, J. R.: Correction of ptosis of the thighs: The thigh lift. Plast. Reconstr. Surg., *37*: 494, 1966.
10. Lewis, J. R.: Atlas of Aesthetic Plastic Surgery. Boston, Little, Brown and Co., 1973.
11. McKissock, P. K.: Reduction mammoplasty with a vertical dermal flap. Plast. Reconstr. Surg., *49*:245, 1972.
12. McKissock, P. K.: Mastopexy and the vertical dermal pedicle. *In* Owsley, J. Q., Jr., and Peterson, R. A. (eds.): Symposium on Aesthetic Surgery of the Breast. St. Louis, C. V. Mosby Co., 1978.
13. Pitanguy, I.: Trochanteric lipodystrophy. Plast. Reconstr. Surg., *34*:280, 1964.
14. Pitanguy, I.: Abdominal lipectomy: An approach to it through an analysis of 300 consecutive cases. Plast. Reconstr. Surg., *40*:384, 1967.
15. Pitanguy, I.: Dermolipectomy of abdominal wall, thighs, buttocks, and upper extremity. *In* Converse, J. M. (ed.): Reconstructive Plastic Surgery. Philadelphia, W. B. Saunders Co., 1977.
16. Rebello, C., and Franco, T.: Abdominoplastia pela incisio sub-mamania. Rev. Bras. Cin., *7*:249, 1972.
17. Strombeck, J. O.: Mammoplasty: Report of a new technique based on the two pedicle procedure. Br. J. Plast. Surg., *13*:79, 1960.
18. Strombeck, J. O.: Reduction mammoplasty. *In* Grabb, W. C., and Smith, J. W. (eds.): Plastic Surgery. Boston, Little, Brown and Co., 1973.
19. Weiner, D. L., Aiache, A. E., Silver, L., et al.: A single dermal pedicle for nipple transposition in subcutaneous mastectomy, reduction mammoplasty or mastopexy. Plast. Reconstr. Surg., *51*:115, 1973.
20. Wise, R. J.: A preliminary report on a method of planning the mammoplasty. Plast. Reconstr. Surg., *17*:367, 1956.

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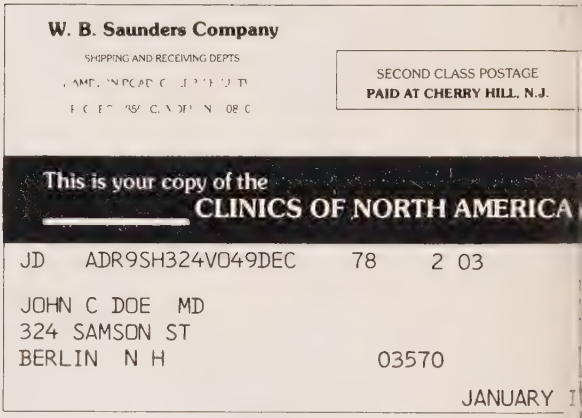

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